A LEADING BIOTECH IN THE DEVELOPMENT OF GAME-CHANGING MICROBIOME-BASED BIOTHERAPIES

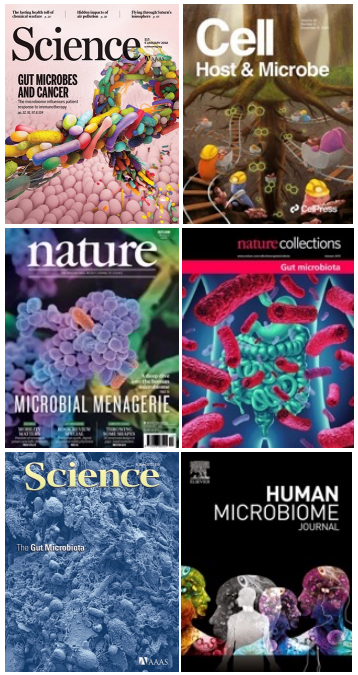
September 2021

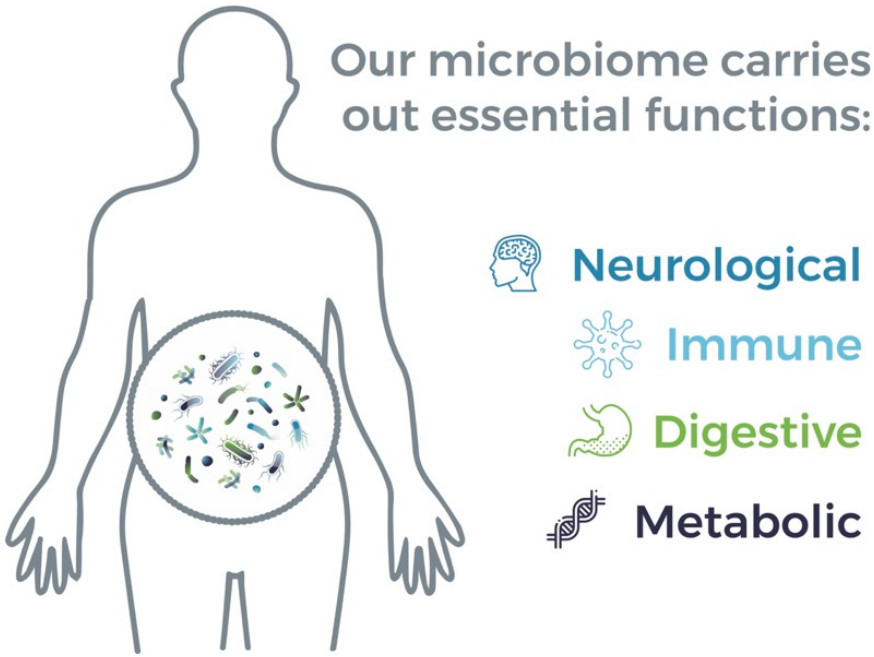
YSOPIA bioscience

Unleashing microbiome-based therapies

Because a Majority of Diseases Start in the Gut, What if We Could Address Them in a New Way with Microbiome-Based Therapeutic Approaches?

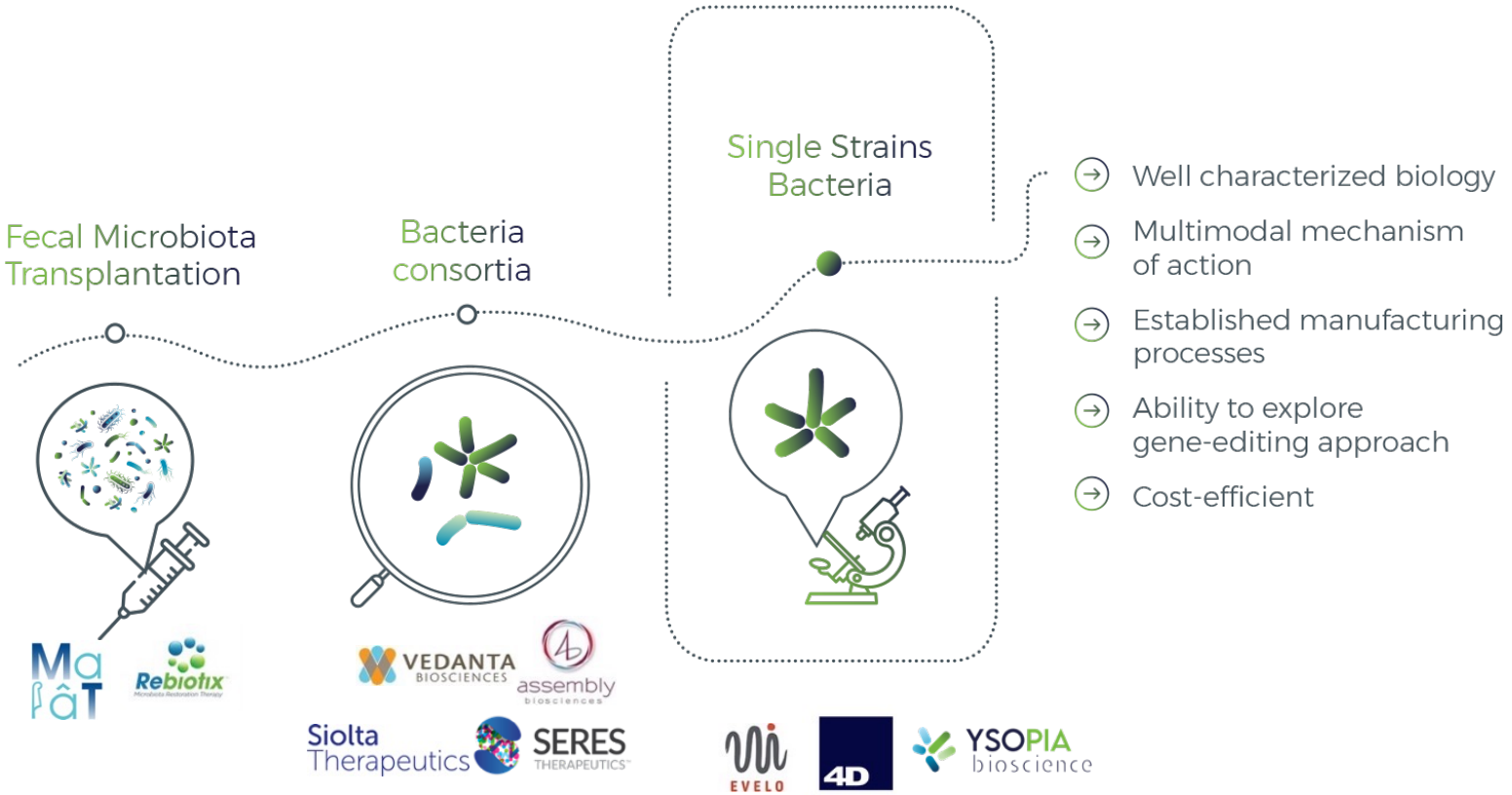
Strong body of scientific evidence has shown that gut microbiome dysbiosis is at the root of numerous diseases





The Development of Microbiome-Based Therapies is the New Paradigm in Medicine

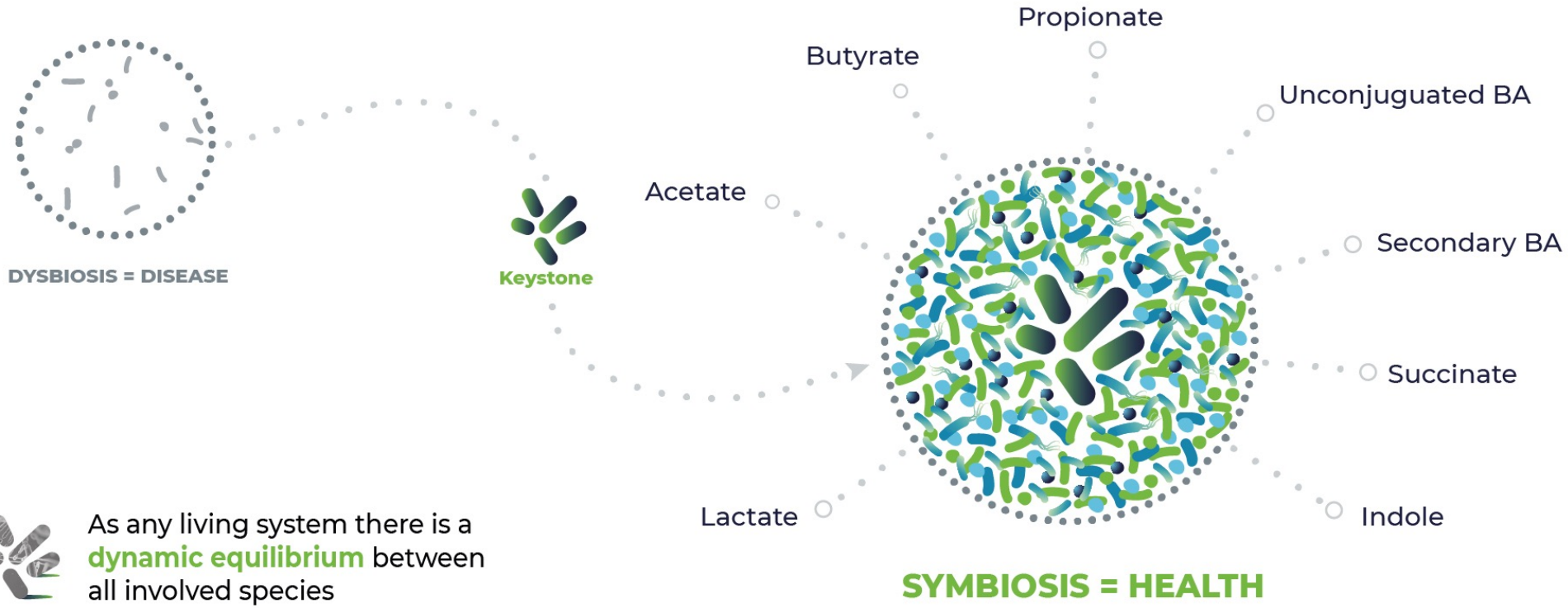
The Gut Microbiome Field Combines Scientific and Clinical Validation



YSOPIA reaps benefits from a differentiating competitive positioning: Single-Strain Keystone Bacteria

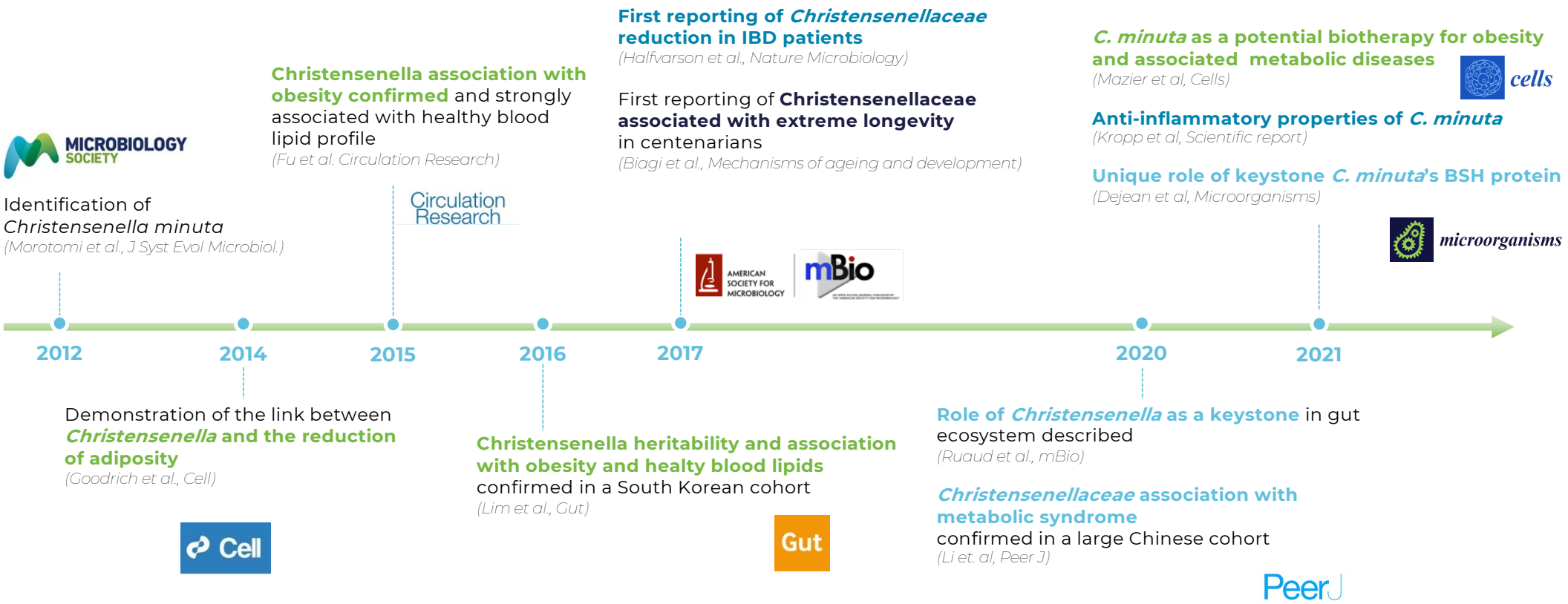
Leveraging the Power of Keystone Single-Strain Bacteria

Each ecosystem has its own **keystone species having a major influence on their environment.**
Loss of keystone bacteria impacts the key functions of the host.



As any living system there is a **dynamic equilibrium** between all involved species

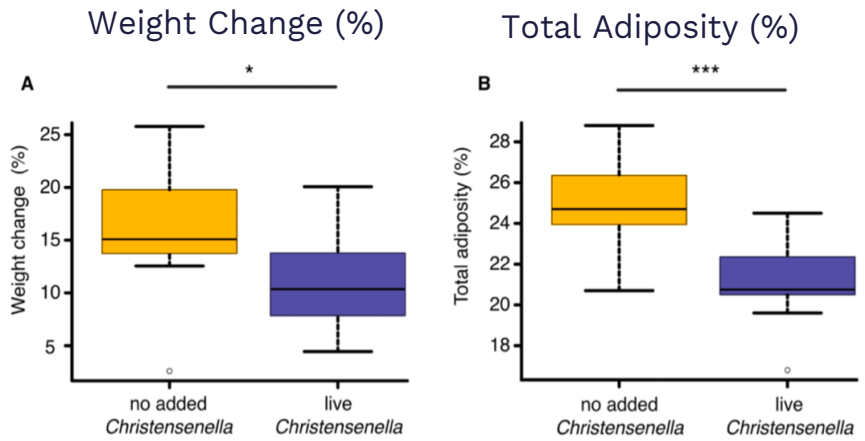
Strong Scientific Rationale Linking Christensenella to Disease Development



YSOPIA is the first biotech company to harness the tremendous therapeutic potential of *Christensenella*

Christensenella Prevents Obesity in Animal Models

Transplantation of *C. minuta* in germ-free mice demonstrated lower body fat percentage and lesser weight gain



- **Obesity has been associated with a loss of christensenella bacteria in numerous international scientific publications**
- **People with higher amounts of *Christensenella minuta* tend to be leaner (Cornell University)**

Peters et al. Scientific Reports 2018, Goodrich et al. Cell 2014

Targeting gut microbiome emerged as the most promising opportunity to treat obesity

OBESITY
recognized as a pandemic in 1997

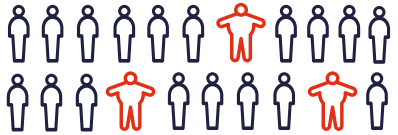
World Health Organization

650 million
OBESE ADULTS
over the world

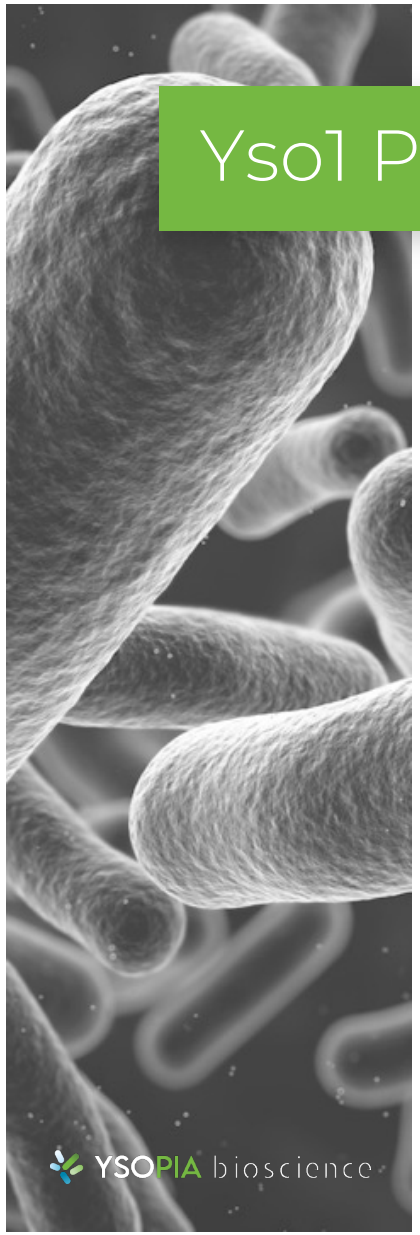
124 million
OBESE CHILDRENS
& ADOLESCENTS
in 2016

OBESITY x3
SINCE 1975

By 2025,
1 billion people
will be
living with
OBESITY



WHO, World Obesity Federation



Yso1 Program

Harnessing the potential of *Christensenella minuta* as a novel biotherapy to treat obesity and associated metabolic disorders, called Xla1

- Showed strong efficacy results in preclinical animal models
- Phase 1 clinical trial completed => safety and tolerability profile validated
- Phase 1 full data expected Q4 21

IP secured

Candidate strain selection ongoing

Fully characterized *C. minuta* library

GMP grade production

Human Safety validated

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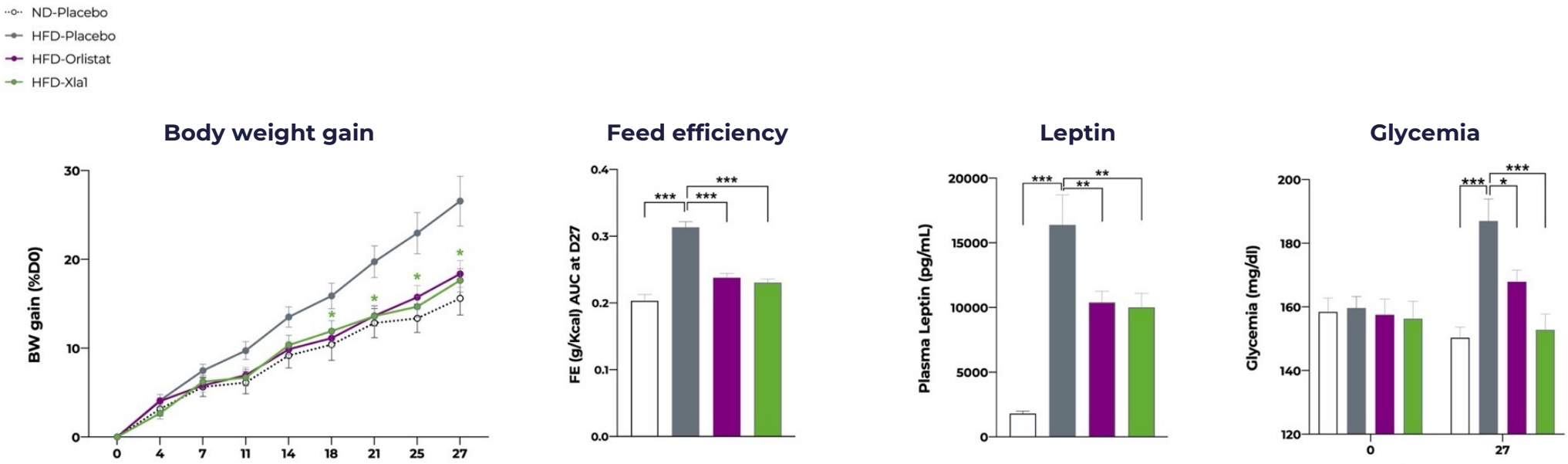
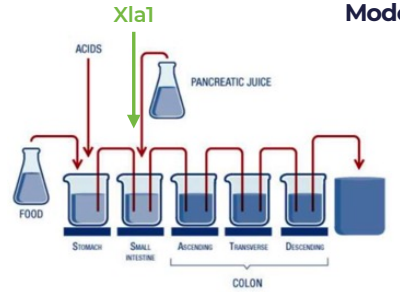
C. minuta Xla1 Mechanism of Action in Obesity



In mice on high fat diet for 4 weeks, Xla1 reduced body weight gain significantly as well as food efficiency, circulating leptin levels and normalized glycemia

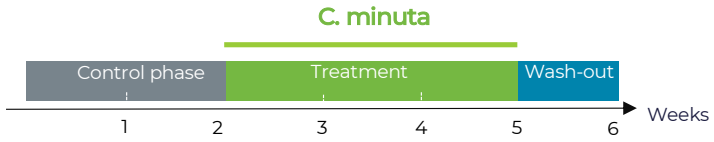
YSOPIA Bioscience, Mazier et al., Cells 2021, 10, 823

Xla1 restores gut microbiome symbiosis *ex vivo*



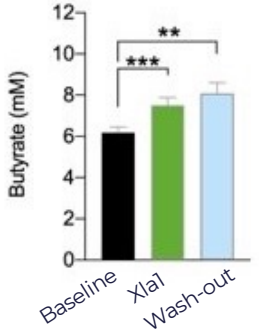
SHIME: In vitro gut microbiome model

Modelling Xla1 effects on human gut microbiome

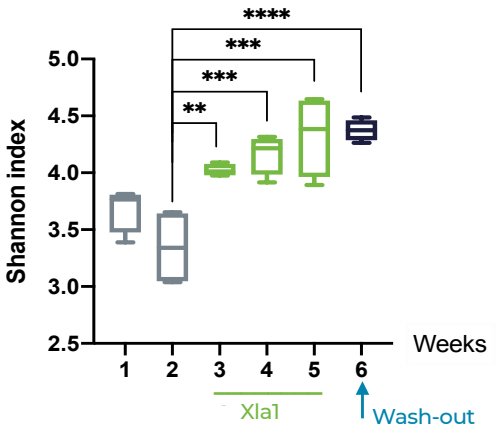


- Culturing the dysbiotic microbiome of patients
- Adding Xla1
- Measuring whether Xla1 restores symbiosis

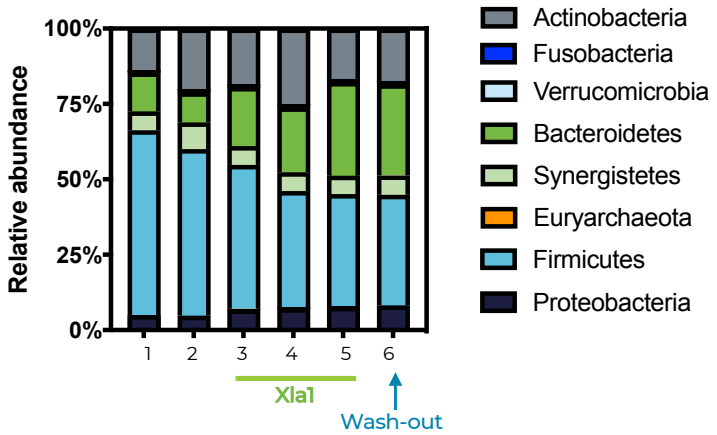
Xla1 increases butyrate levels



Xla1 restores microbiome diversity



Xla1 increases Bacteroidetes/Firmicutes ratio*



* The Bacteroidetes/Firmicutes ratios is decreased in obese patients

Mazier et a; Cells, 2021

CAUSALITY Phase 1 Clinical Study

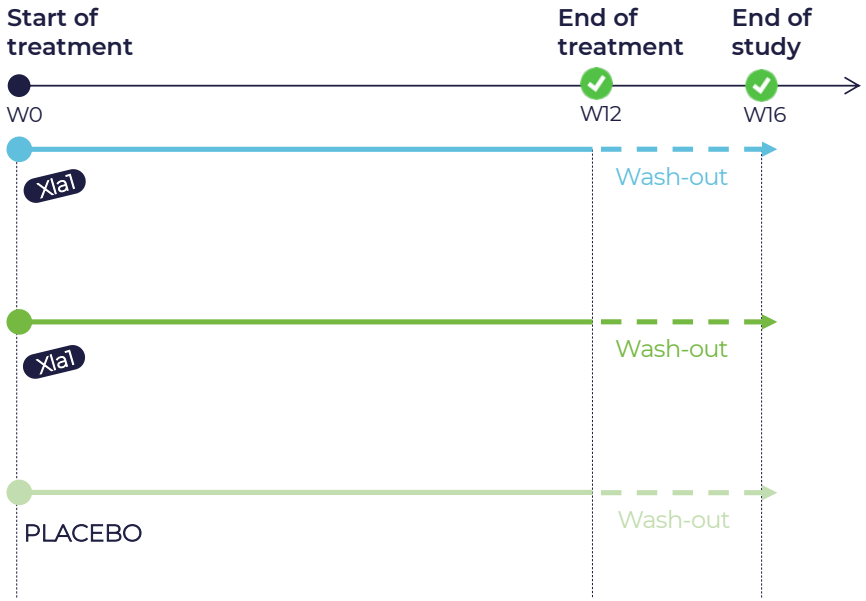
Excellent Safety and Tolerability Profile Demonstrated

- Primary endpoint: Assess the **safety and tolerability of Xla1** *
- Secondary endpoints: Evaluate the effects of Xla1 on subject's intestinal **microbiome ecology** and the **engraftment dynamics** of Xla1 in the gastrointestinal tract
- Dosing Strategy: 1 capsule daily during 3 months
- Study protocol: Randomized, placebo-controlled, double-blind

ARM 1: HEALTHY VOLUNTEERS
n=8
BMI: 18.5-25

ARM 2 a: OBESE VOLUNTEERS + Xla1
n=20
BMI: 25-35
1 metabolic abnormality

ARM 2 b: OBESE VOLUNTEERS + placebo
n=10
BMI: 25-35
1 metabolic abnormality



CAUSALITY SAFETY DATA

Similar occurrence of side effects both in Xla1 and placebo groups

- No Serious Adverse Event
- No subject discontinued due to Adverse Events
- No Adverse Event related to biochemical biomarkers

*Xla1 is the Drug Product from *C. minuta* strain

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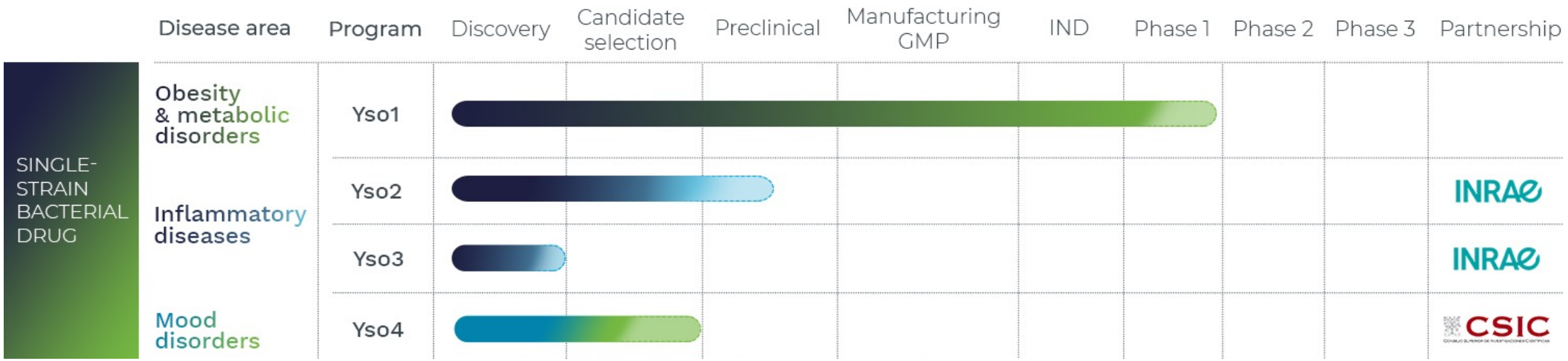
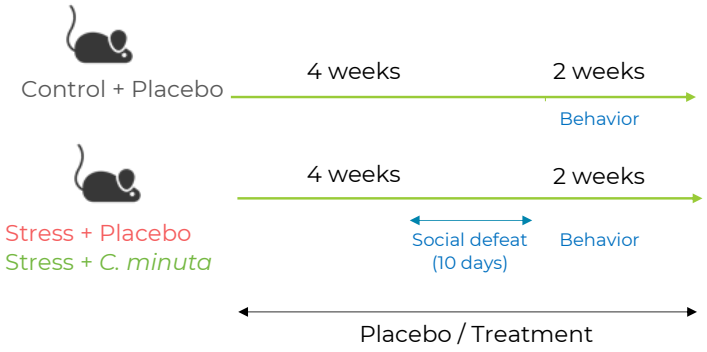
Developing Single-Strain Bacteria as Effective Biotherapies for Multiple Disease State

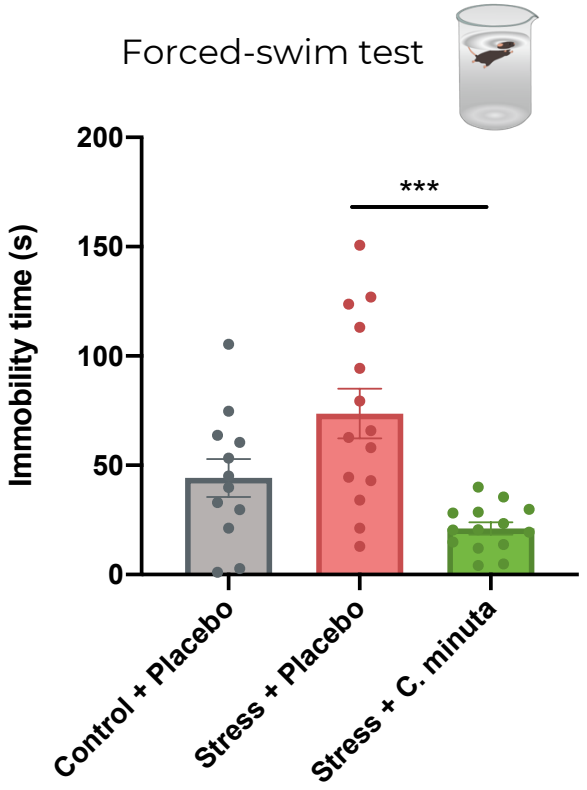


Exploring additional therapeutic areas with high unmet medical needs, such as **oncology**

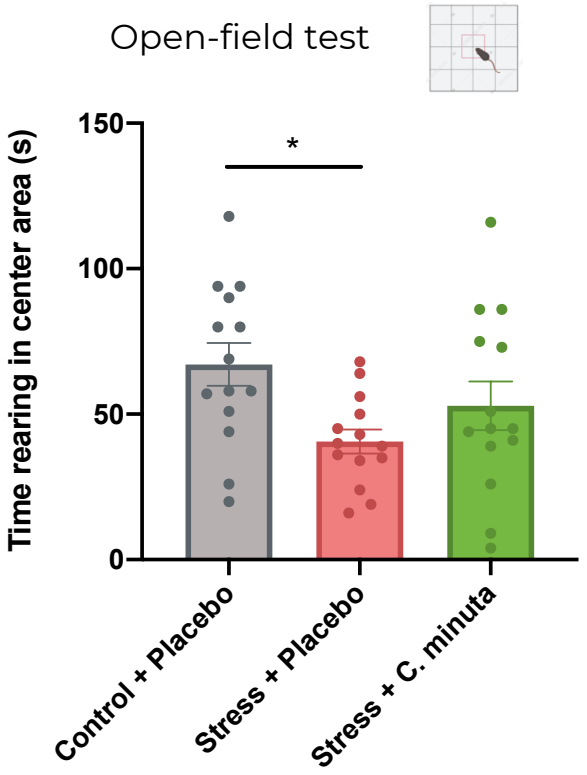
C. minuta Restores Depressive-like Behaviors



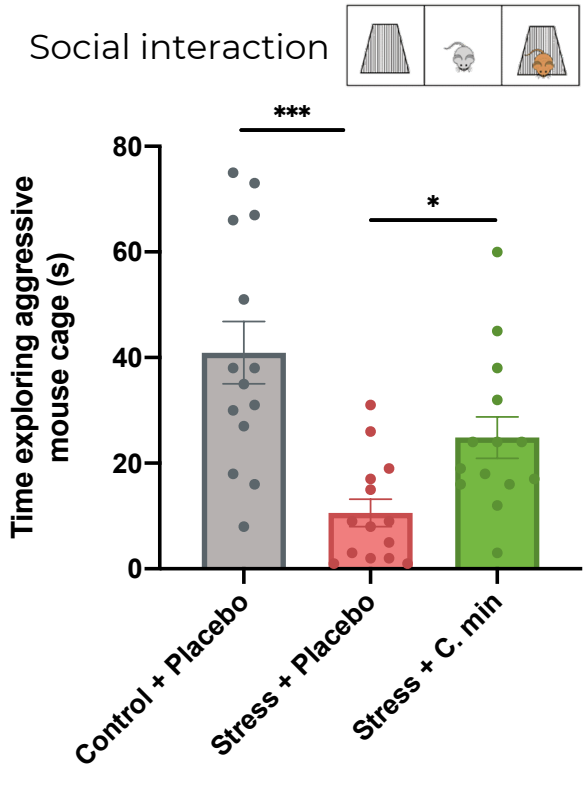
Forced-swim test



Open-field test

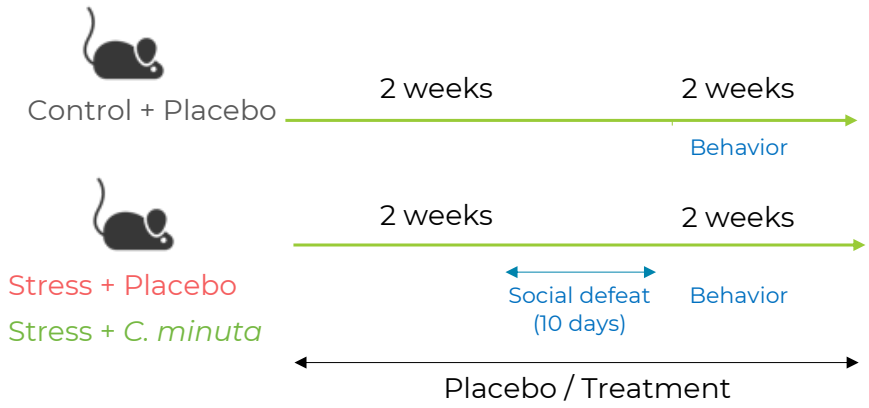


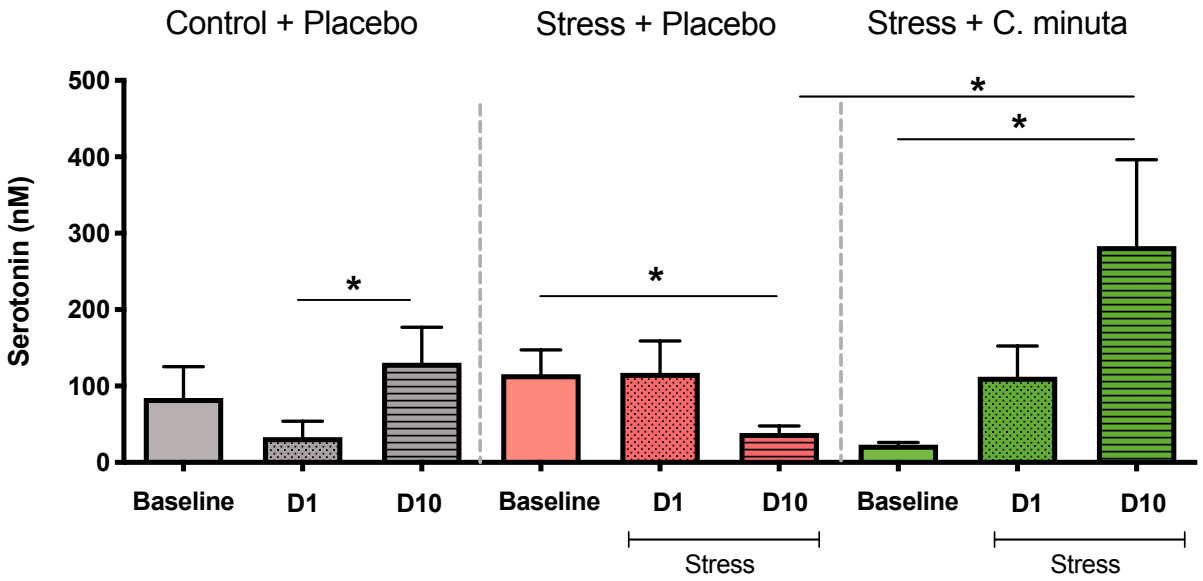
Social interaction



Treatment with *C. minuta* restores the depression-like behavior induced by 10 days social defeat

C. minuta Modulates Plasma Levels of Stress Markers and Neurotransmitters





Treatment with *C. minuta* increases plasma levels of serotonin during chronic social defeat

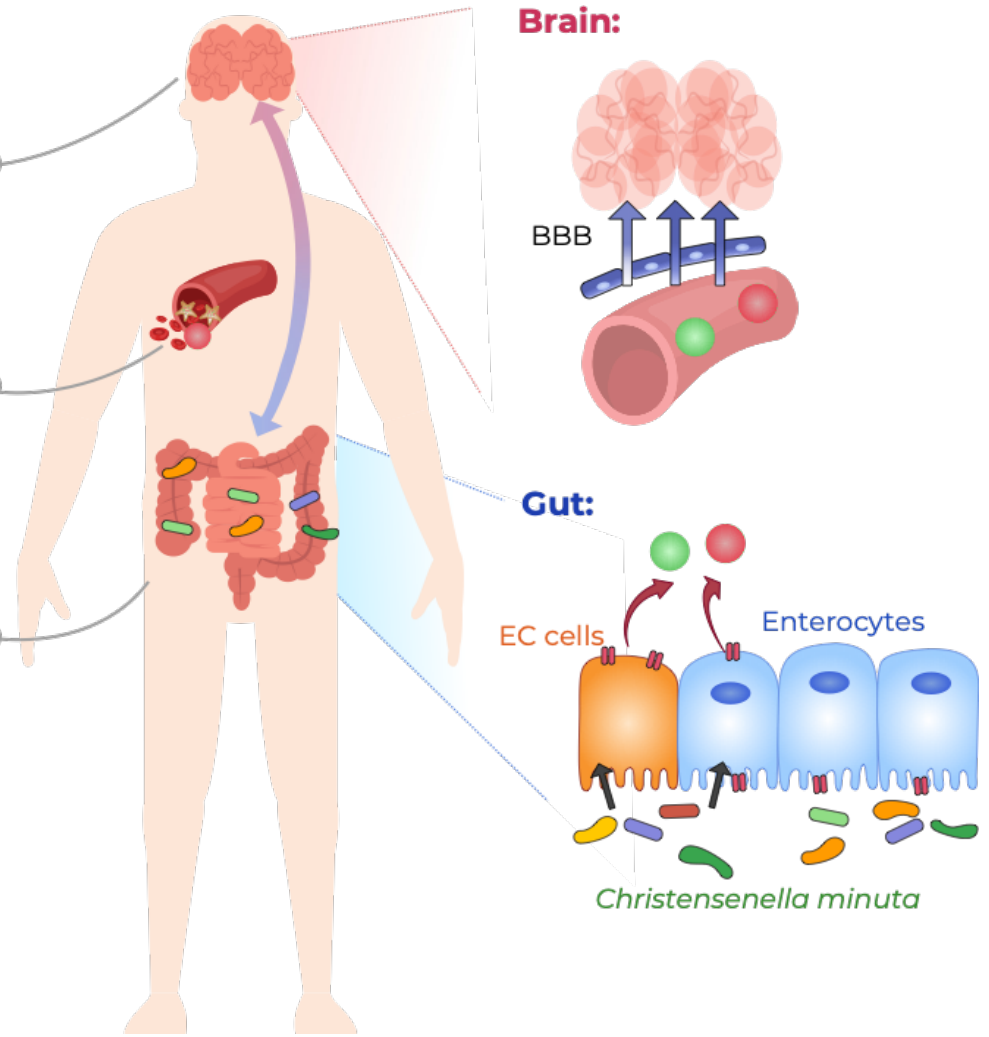
Plasma samples were taken the day before Social Defeat (SD) started / 1 and 10 days after beginning of SD

Build a First-in-Class Biotherapy for Depression

C. minuta to treat depression

Christensenella minuta

- Improves behavior after social defeat in mice
- Reduces inflammation in *in vitro* and *in vivo* models
- Changes neurotransmitters levels in mice blood
- Modifies the microbiome in its whole



Alliance • Promotion • Microbiote

APM aims to position France as a European leader in the development, production and marketing of scientific and therapeutic innovations linked to the **microbiota**

APM brings together more than 20 members, coming from both public and private sectors: Bioaster, Biocodex, Biofortis Mérieux NutriSciences, Biose Industrie, Cynbiome, Da Volterra, Eligo Bioscience, Everimmune, GMT, INRAE, INSERM, Lallemand, Lyonbiopôle, MaaT Pharma, Medicen, Microbiome Foundation, Nexbiome, Novobiome, Pharmabiotic Research Institute, Seventure Partners, Stellate, TargEDys, Ysopia Bioscience.

THANK YOU TO OUR PARTNERS

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INRAE

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Consejo Superior de Investigaciones Científicas

Prof. Yolanda Sanz & her team

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