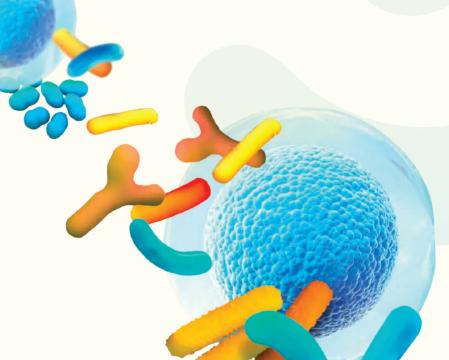
### **GUT** Preclinical Research

INNOVATIVE MODELS TO EXPLORE GUT- ORGANS INTERACTIONS AND ACCELERATE PRODUCT DEVELOPMENT

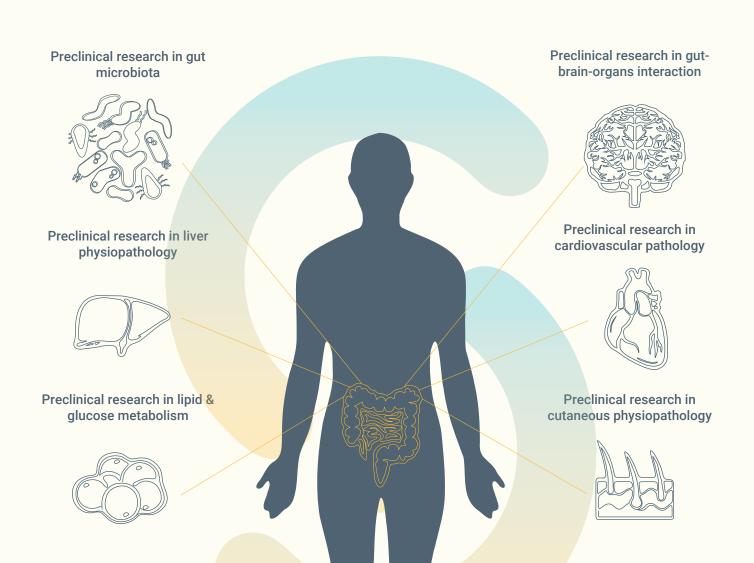




# BEYOND PRECLINICAL TESTING A TRUE RESEARCH PARTNER

Enterosys specializes in preclinical testing with an integrated physiology approach, focusing on the gut-organs axis to deliver tailored solutions for translational research. We support R&D teams throughout the entire development chain, providing *in vitro* and *in vivo* models specifically designed to assess the impact of nutraceuticals, pharmaceuticals, food & feed ingredients, and dermocosmetics.

More than just a CRO, we are a true **research partner**, offering expert guidance and cutting-edge models to optimize product testing, whether for compound **valorization or proof-of-concept validation**. Our gut-centered studies provide personalized support at every stage, ensuring precise and actionable insights to accelerate your innovation.



### TEST YOUR COMPOUNDS WITH ENTEROSYS

#### **NUTRACEUTICALS**

The gut is the gateway for nutraceuticals and their primary site of action. **Probiotics, prebiotics and other functional ingredients** directly modulate the microbiome and metabolic or immune responses.

A gut-centered approach provides robust data to support product development and market claims.





#### **PHARMACEUTICALS**

The gut is a primary absorption gateway and dynamic metabolic regulator, shaping drug bioavailability and overall efficacy. Its barrier, microbial and immune activities exert body-wide effects on energy balance, inflammation and tissue resilience. Integrating gut-focused testing early in development expedites the optimisation of candidate drugs across a broad range of therapeutic areas.

#### **FOOD & FEED**

Functional nutrition is a cornerstone of the **one health approach**, linking human and animal well-being through gut health. Functional foods and feed shape the microbiome, influence digestion, and regulate metabolism, impacting both nutritional efficiency and disease prevention.





#### **NUTRICOSMETICS**

The gut-skin axis is a key player in skin health, highlighting the need for an inside-out (IN & OUT) approach in dermatology. Gut & microbiota regulate inflammation, hydration, and aging, influencing skin condition from within. Our models help evaluate the gut's role in skin homeostasis, opening new avenues for innovation in dermatology.

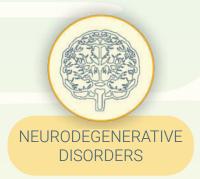
#### REPRODUCING LEAKY GUT

# THE KEY TO PREVENT DISORDERS

The gut plays a central role in systemic health, influencing multiple organs and physiological processes. Our models help you assess the impact of your molecules on gut function and its communication with key organs involved in gastrointestinal, neurodegenerative, dermatological, and metabolic disorders.



The gut is an interactive hub where motility, barrier integrity, microbiota and immunity meet. The leaky gut allows toxins into the bloodstream, sparking body-wide inflammation. Rebuilding barrier strength and microbial balance is therefore pivotal for both prevention and therapy.



The gut-brain axis links microbiota, immune signals and the vagus nerve to the CNS. Dysbiosis fuels neuro-inflammation, disrupts neurotransmitters and weakens the gut barrier.



Energy balance relies on constant dialogue between the gut, its microbiota and peripheral organs. When dysbiosis or barrier damage disrupts this exchange, inflammatory signals rise, insulin action falters and fat stores expand. The gut speaks through many messengers, microbial metabolites (SCFAs, indoles), enteroendocrine hormones (GLP-1, PYY), microbiotamodified bile acids and immune mediators, which together shape appetite, glucose handling, lipid storage and systemic inflammation. This makes the intestine a pivotal target for preventing and treating metabolic disorders.

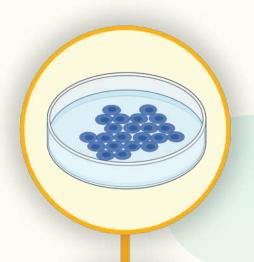


Skin mirrors the gut: dysbiosis and a leaky barrier drive systemic and cutaneous inflammation, hormone disruption and weaker skin resilience, fueling acne, psoriasis, eczema and rosacea. Strengthening microbiome diversity and tight-junctions with inside-out nutraceuticals and microbiome-friendly topicals calms flares, modulates immunity and slows skin ageing, matching the demand for holistic "beauty from within."

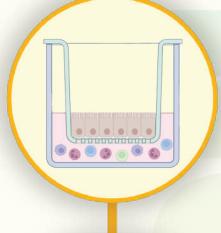
#### **IN VITRO MODELS**

#### 1- Choose your cell type and immune conditions

At Enterosys, we offer a comprehensive range of *in vitro* models, from 2D cell cultures to engineered microtissues. Each model is designed to meet specific R&D needs, with varying levels of physiological integration and representativeness.



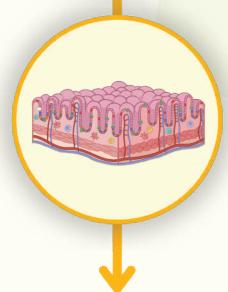
Cell type	Function
HT29 (human)	Gut barrier function
HT29-MTX (human)	Mucus production
Caco-2 (human)	Absorptive function
STC-1 (mouse)	Endocrine function



#### Inflammatory response (co-culture)

THP1 (human)	Monocytic cell line
PBMC (human)	Primary cells*

<sup>\*</sup> Due to interindividual variability, our primary cultures are conducted using five different donors, each tested in triplicate to ensure robust and representative results.



Cell type	Function
Engineered microtissues (human)	Integrated intestinal functions

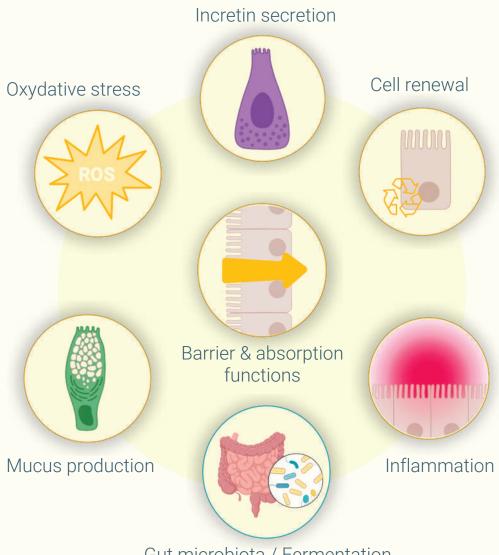
#### **IN VITRO MODELS**

#### 2- Choose your cell challenge

Cell challenge	Phenotype
LPS	Dysbiosis
TNF-α	Inflammation
Ovalbumin	Food allergy
Gliadin	Gluten intolerance



#### 3- Choose your cell function



Gut microbiota / Fermentation

#### **IN VIVO MODELS\***

#### 1- Choose your murine model

Pathology phenotype		Model
Colitis and recover	у	DSS
Diarrhea	Acute	Castor oil
	Chronic diarrhea associated with antidiabetic treatment	Metformin
	Allergy-induced diarrhea	Ovalbumin
	Secretory diarrhea	Bile acids
constipation	Pharmacological constipation	Loperamid
	Adsorption-based constipation	Activated charcoal
Leaky gut		Hight Fat Diet (HFD)



#### Looking for a different model? Contact us!

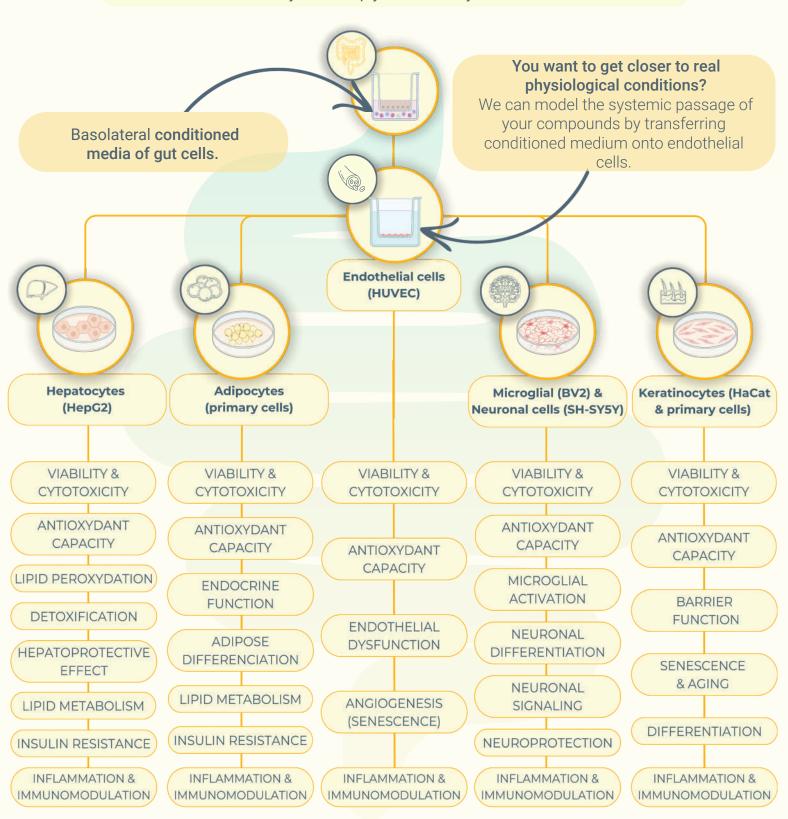
Our scientific expertise allows us to develop custom-made models tailored to your specific needs, ensuring the most relevant and impactful results for your research.

<sup>\*</sup>In strict accordance with the ethical protocols validated by the national ethics committee, in compliance with the 3R rule and under official veterinary supervision.

#### DECODING GUT-ORGAN IN VITRO CROSS-TALK

## A MULTI-AXIS APPROACH TO HOLISTIC HEALTH

Choose the gut-organ axis that matters to you and discover the **read-outs where**Enterosys can help you evaluate your actives.

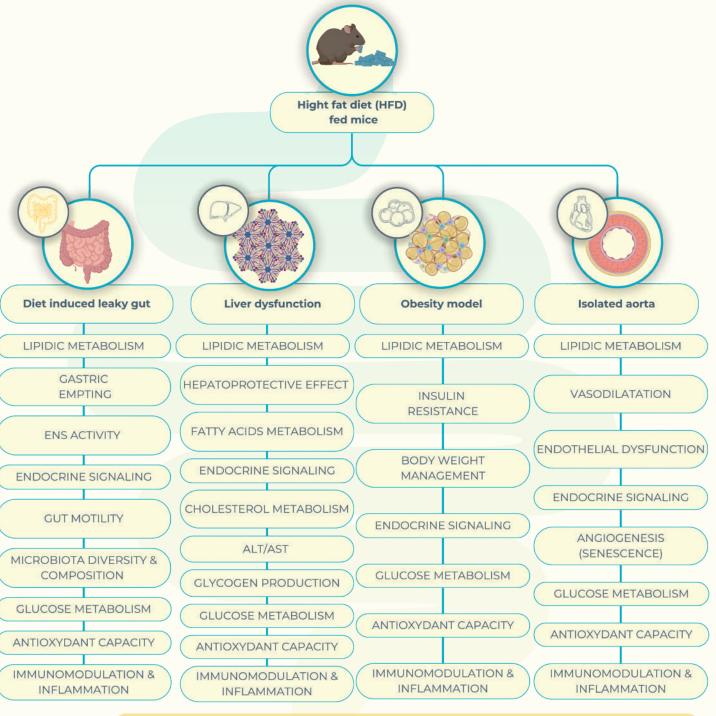


We can evaluate your active ingredients without the intestinal compartment, ensuring a broader and more flexible testing approach.

#### DECODING GUT-ORGAN IN VIVO CROSS-TALK

## A MULTI-AXIS APPROACH TO HOLISTIC HEALTH

Choose the gut-organ axis that matters to you and discover the **read-outs where**Enterosys can help you evaluate your actives.





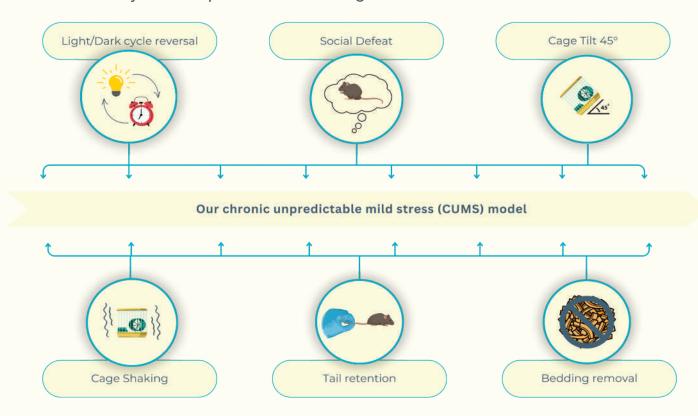
#### Looking for a different readout? Contact us!

Our scientific expertise allows us to develop custom-made protocols tailored to your specific needs, ensuring the most relevant and impactful results for your research.

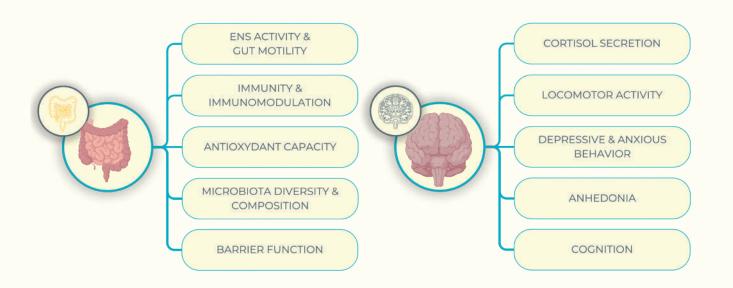
#### DECODING GUT-BRAIN IN VIVO CROSS-TALK

# A MULTI-AXIS APPROACH TO MENTAL HEALTH

Leverage our specialized *in vivo* models to investigate the **gut-brain relationship and** measure the efficacy of your active ingredients. By integrating physiological, behavioral, and molecular endpoints, these models provide robust insights into how your compounds influence gut-brain axis function.



Choose the UCMS read-outs where Enterosys can test your active's neurobehavioral and systemic effects.



### FROM EXPERIMENTAL INSIGHTS TO THERAPEUTIC DEVELOPMENT

# A CUSTOMER FOCUSED JOURNEY DRIVEN BY YOUR GOALS



Setting the stage for phenotype-driven personalized medicine.

**Designing go/no-go** experimental protocols tailored to meet your specific research objectives.

Creating comprehensive study reports with infographics and complementary experiments to maximize the impact of your results.

### OUR MOST RECENT CO-PUBLICATIONS WITH OUR CLIENTS

Pasteurized Akkermansia muciniphila improves glucose metabolism is linked with increased hypothalamic nitric oxide release.

Abot A, Brochot A, Pomié N, Astre G, Druart C, de Vos WM, Knauf C, Cani PD. Heliyon. 2023 Jul 13;9(7):e18196. doi: 10.1016/j.

Camu-Camu Reduces Obesity and Improves Diabetic Profiles of Obese and Diabetic Mice: A Dose-Ranging Study. Metabolites.

Abot A, Brochot A, Pomié N, Wemelle E, Druart C, Régnier M, Delzenne NM, de Vos WM, Knauf C, Cani PD. 2022 Mar 29;12(4):301. doi: 10.3390/metabol2040301.

Effect of the dietary supplement PERMEAPROTECT+ TOLERANCE® on gut permeability in a human co-culture epithelial and immune cells model.

Abot A, Pomié N, Astre G, Cani PD, Aussant J, Barrat E, Knauf C.

Heliyon. 2024 Mar 27;10(7):e28320. doi: 10.1016/j.

Limosilactobacillus reuteri BIO7251 administration improves metabolic phenotype in obese mice fed a high fat diet: an inter-organ crosstalk between gut, adipose tissue and nervous system.

Abot A, Pomié N, Astre G, Jaomanjaka F, Marchand P, Cani PD, Roudier N, Knauf C.

Int J Food Sci Nutr. 2024 Feb doi: 10.1080/09637486.2023.2276672.

Targeting the Enteric Nervous System to Treat Metabolic Disorders? «Enterosynes» as Therapeutic Gut Factors.

Knauf C, Abot A, Wemelle E, Cani PD.

Neuroendocrinology. 2020doi: 10.1159/000500602.

Role of the intestinal microbiota in contributing to weight disorders and associated comorbidities.

Van Hul M, Neyrinck AM, Everard A, Abot A, Bindels LB, Delzenne NM, Knauf C, Cani PD.

Clin Microbiol Rev. 2024 Sep. doi: 10.1128/cmr.00045-23.

### **GUT** Preclinical Research

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