Exploring Novel "Gut Care" Possibilities Using Intestinal Organoids

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Kirin Holdings Company, Limited. KIRIN Central Research Institute

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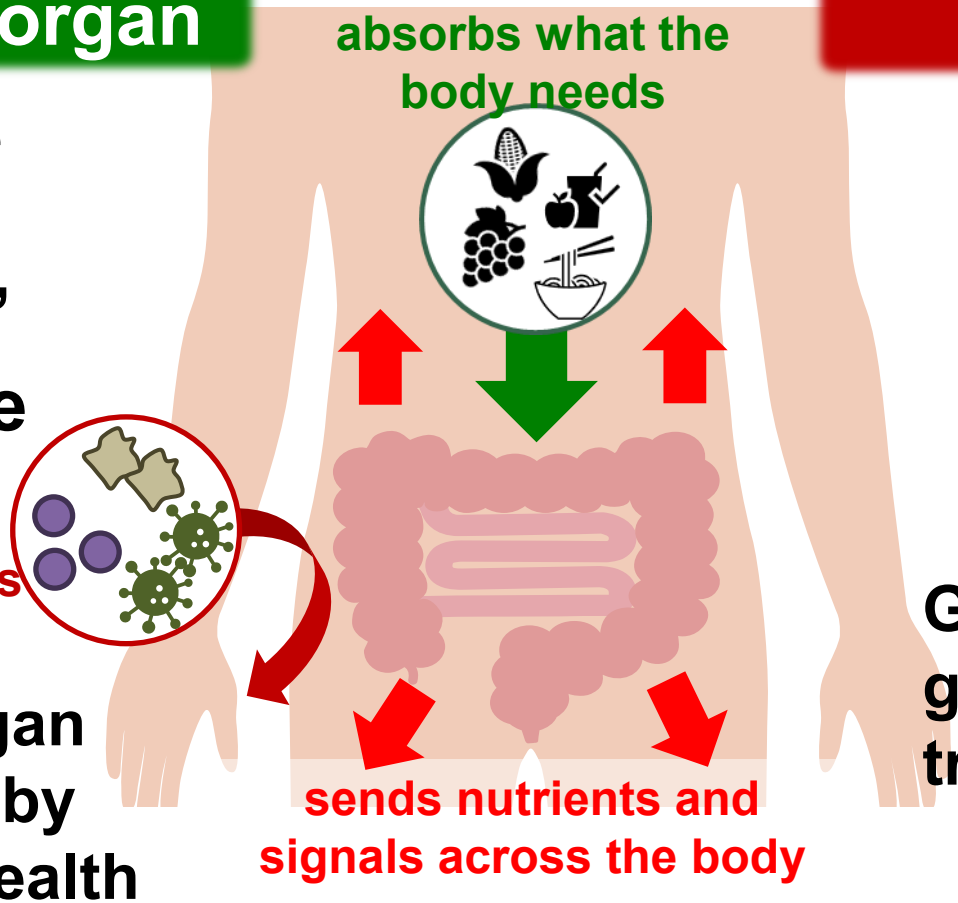
The gut is powerful — and the market is huge

Gut's value as an organ

- Nutrient uptake
- Immune hub
- ”Second Brain”
- Gut microbiome



Existing solutions

Gut-care market is rapidly growing — now on a trillion-yen scale

The gut is a unique organ that can be influenced by diet to help personal health

Many aspects still unknown — scientifically and commercially promising

Limitations of past gut research

✓ Most studies infer gut condition from feces

Nutrients
Food components

Small intestine
Metabolism/absorption

Immunity

Gut microbiome
Secondary metabolism

Large intestine
Water and metabolite absorption

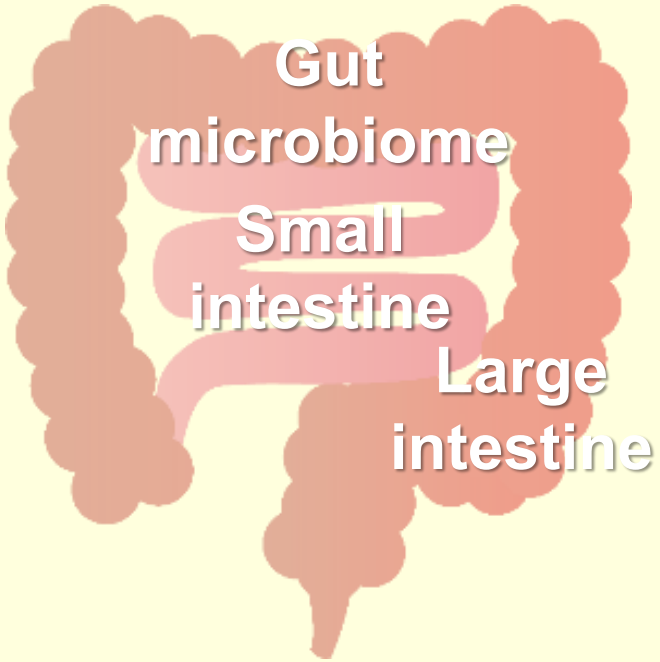
The gut itself has remained largely a black box

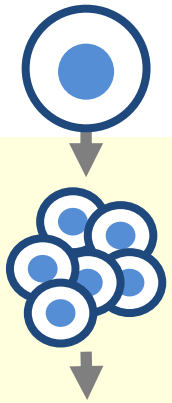
Feces
Leftovers

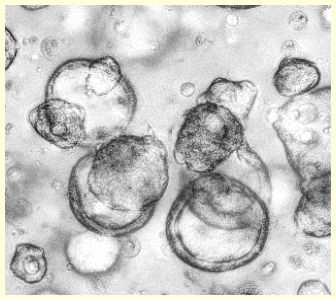
Past focus: stool-based analyses, especially for the large intestine

Organoids let us study gut tissue directly

✓ Organoids: lab-grown mini-organs that mimic human gut tissue







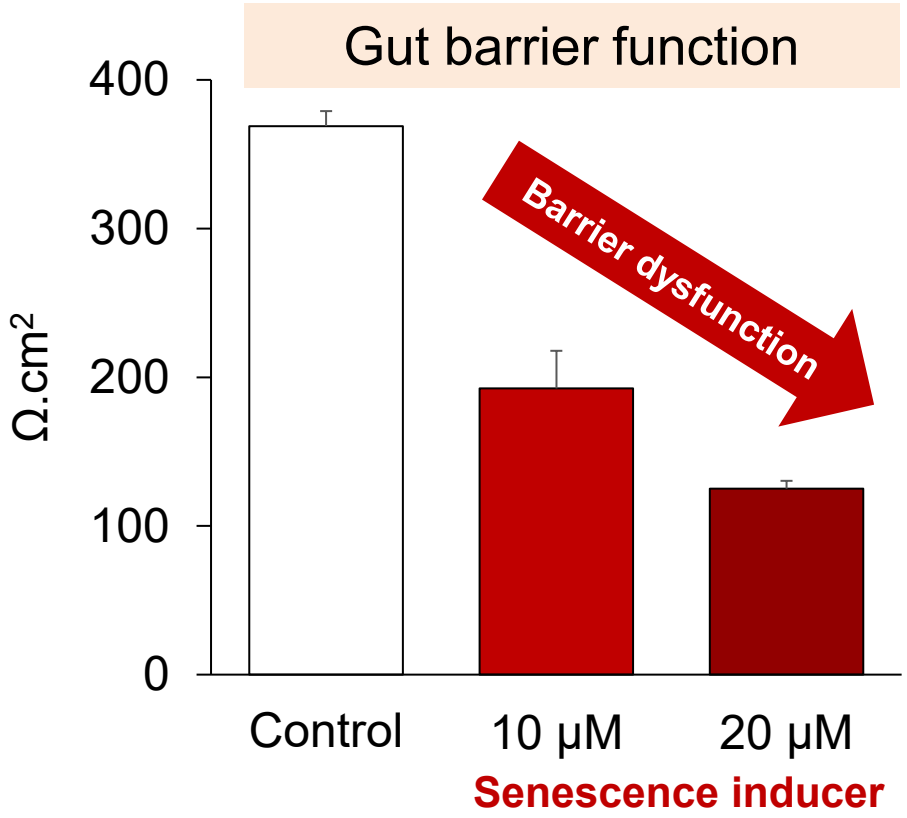
Small intestinal organoids

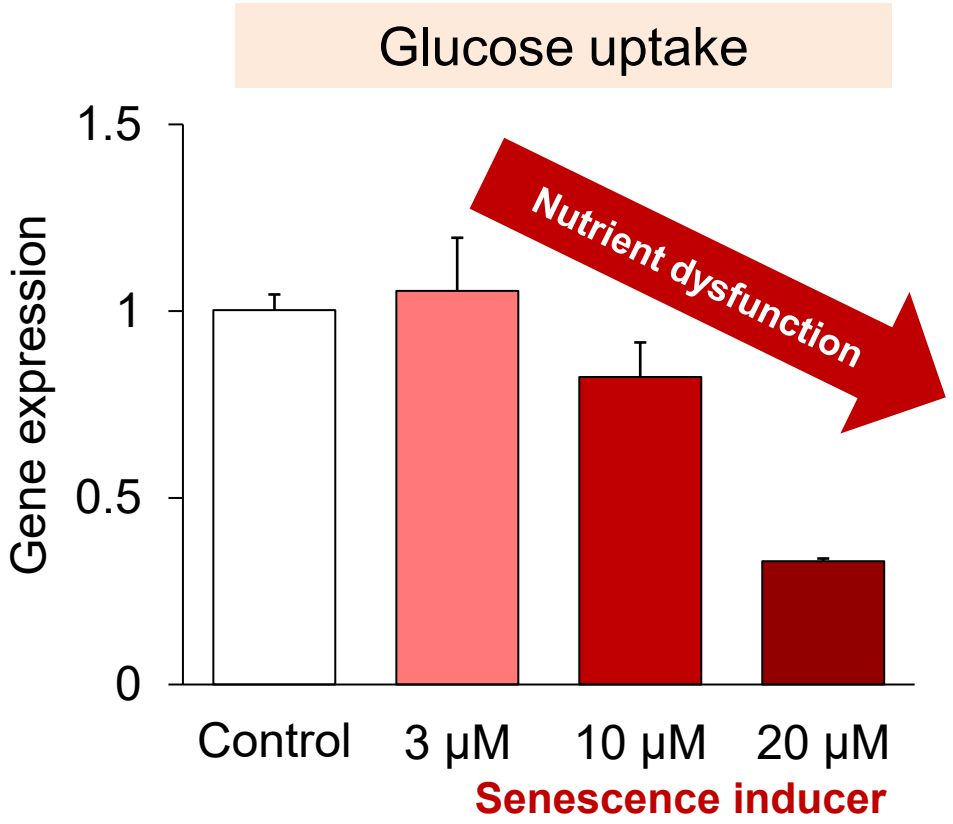
- iPS cell–derived organoids ≈ human small intestine grown in a dish
- This enabled us to test effects on gut tissue in conditions closer to the real human gut

Feces
Leftovers

What organoids make possible

- ✓ Enabled a focuse on **gut aging** as a fundamental health issue
- ✓ Allowed modeling of age-related gut states and measured functional loss

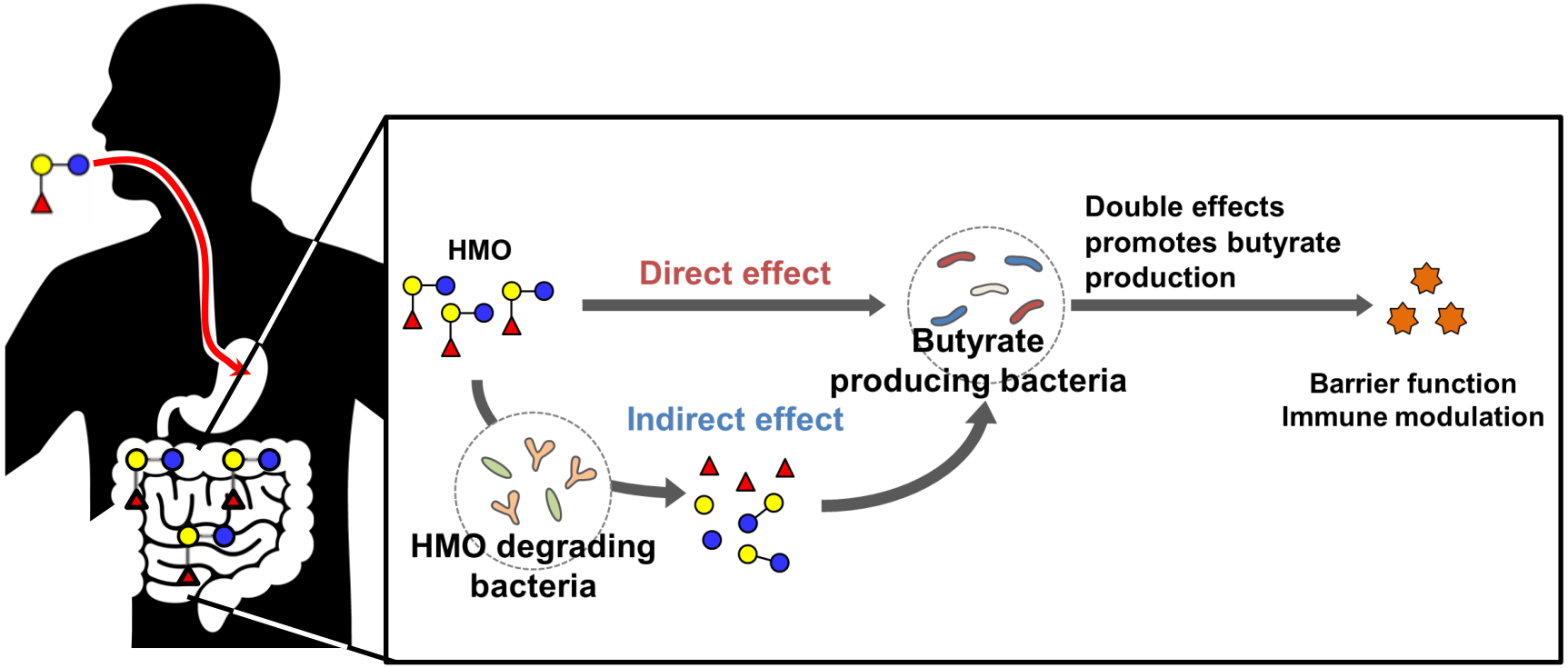


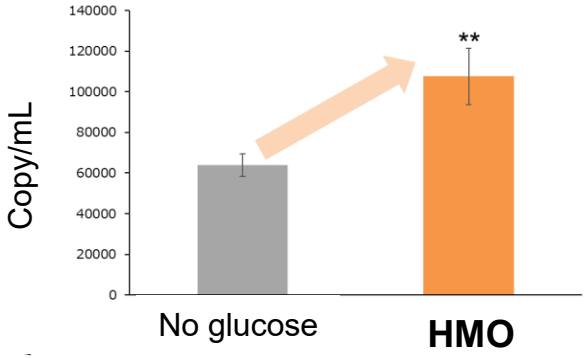


What materials can restore these aging-related changes?

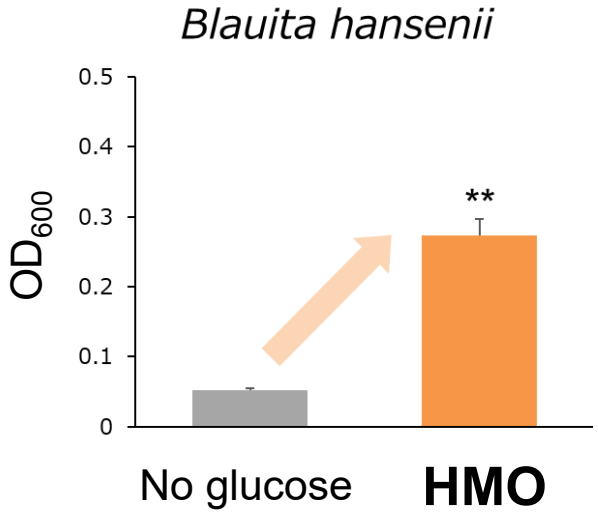
HMO promotes microbial butyrate production

Human milk oligosaccharides (HMOs; components characteristic of breast milk) encourage growth of certain butyrate-producing bacteria





In co-culture with HMO-degrading bacteria, HMO increased counts of *F. prausnitzii*, a butyrate producer



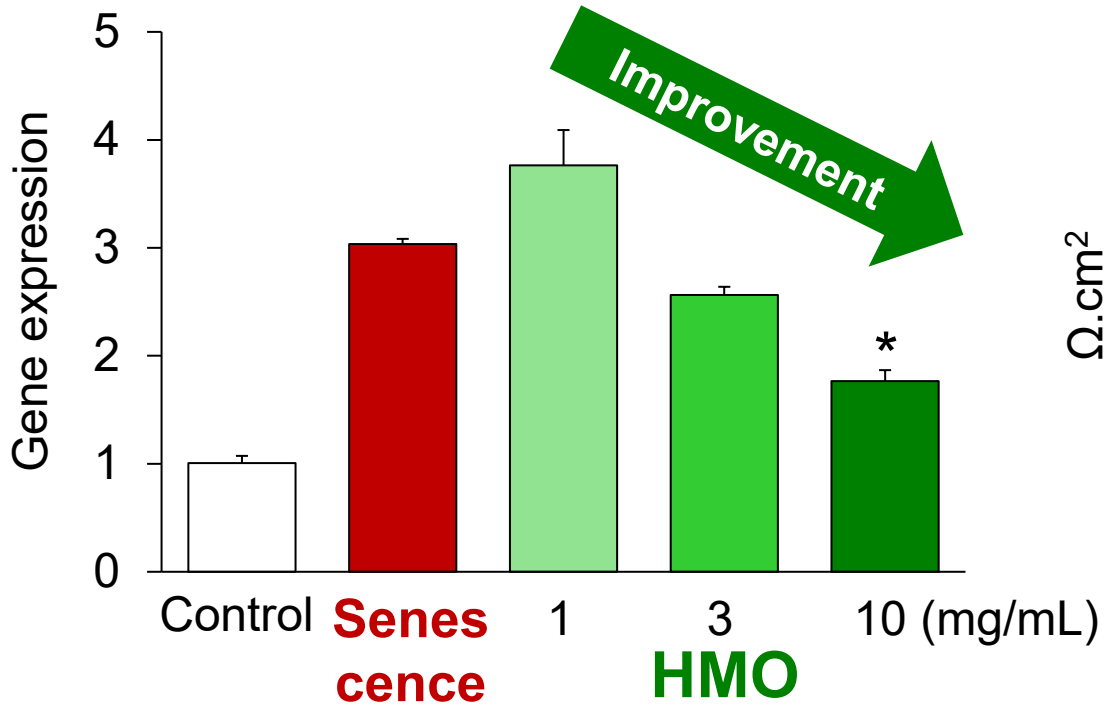
HMO increases certain butyrate-producing bacteria (e.g., increase in genus *Blautia*)

**: Statistically significant vs senescence model ($p < 0.01$)

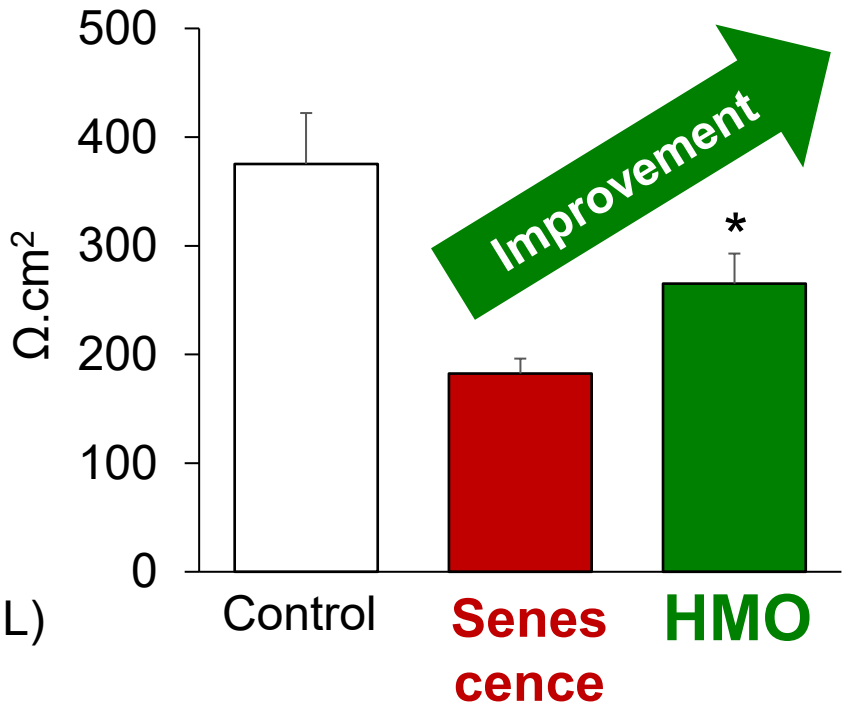
HMO protects the small intestine from aging

✓ In a senescence model, HMO reduced inflammation and improved barrier function

Inflammation



Barrier function



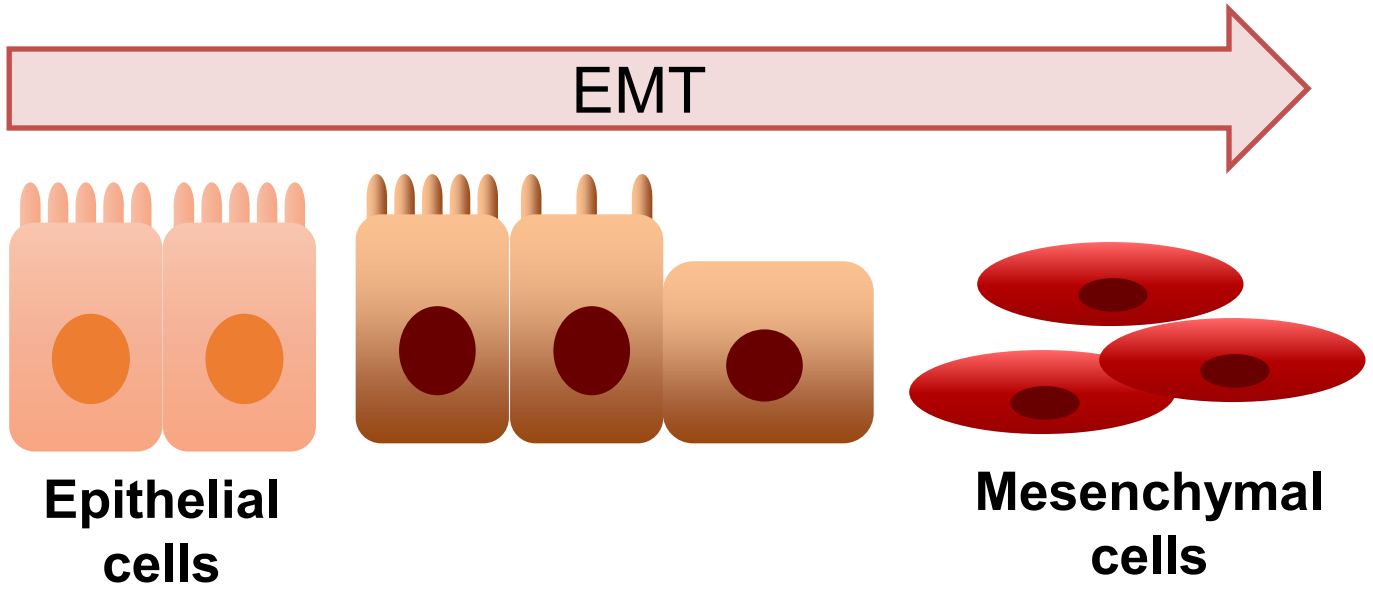
*: Statistically significant vs senescence model ($p < 0.05$)

Although HMO is known as a large-intestine prebiotic,
it also acted directly on small-intestine organoids

Link to aging biology: EMT

✓ We investigated epithelial–mesenchymal transition (EMT), a process linked to aging

EMT: epithelial cells lose their normal traits and shift toward a mesenchymal cell type



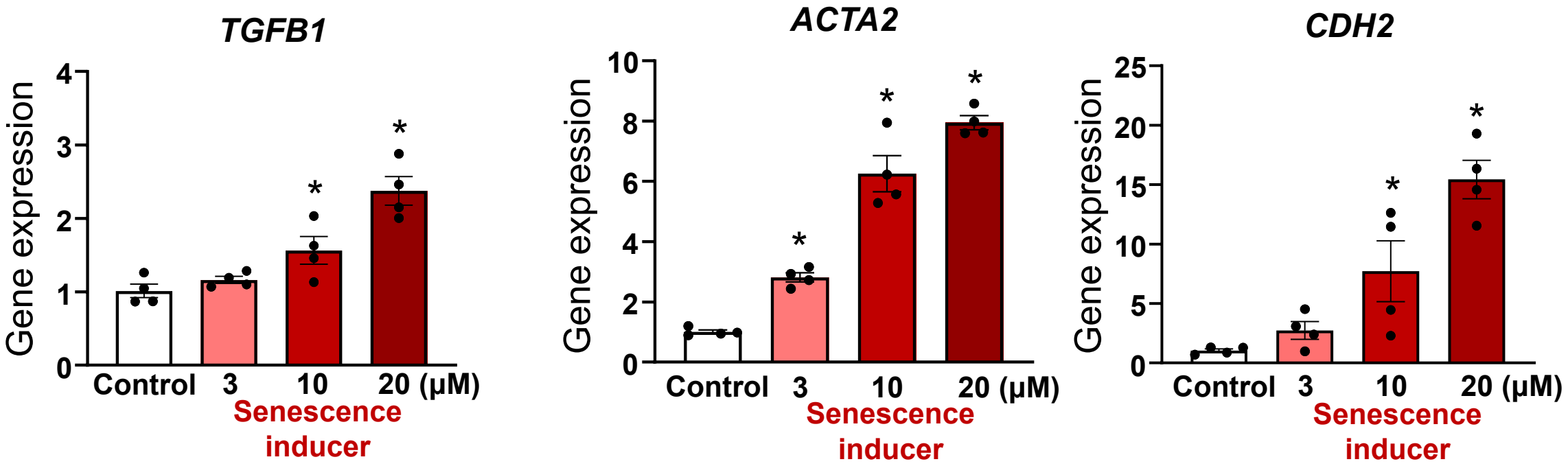
“Changes in extracellular matrix” (including EMT) was added to the Hallmarks of Aging in 2025

EMT occurs in senescent organoids

- ✓ In senescent organoids, EMT marker genes increased
- ✓ Suppression of EMT improved nutrient function, suggesting EMT is a functional target to prevent gut aging

EMT inducing gene

Mesenchymal marker genes

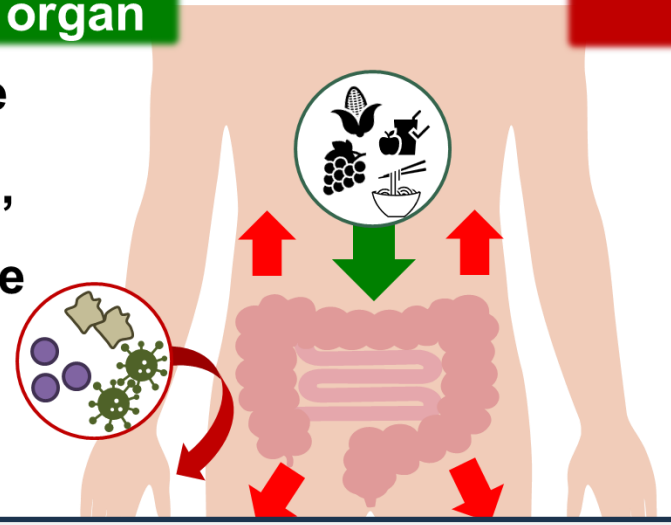


*: Statistically significant vs control group ($p < 0.05$)

Summary — business and scientific value

Gut's value as an organ

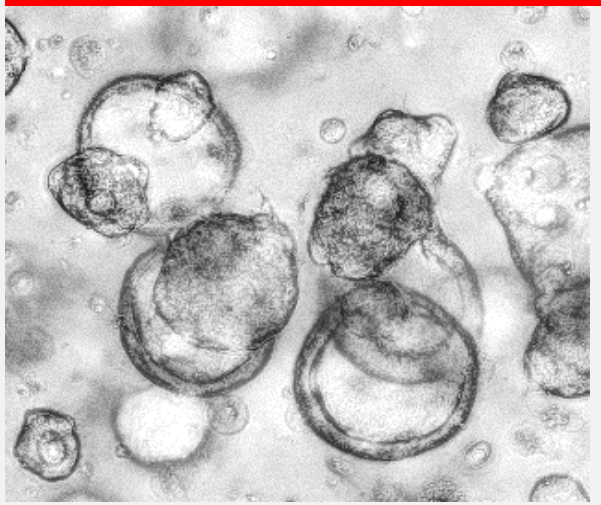
- Nutrient uptake
- Immune hub
- "Second Brain"
- Gut microbiome

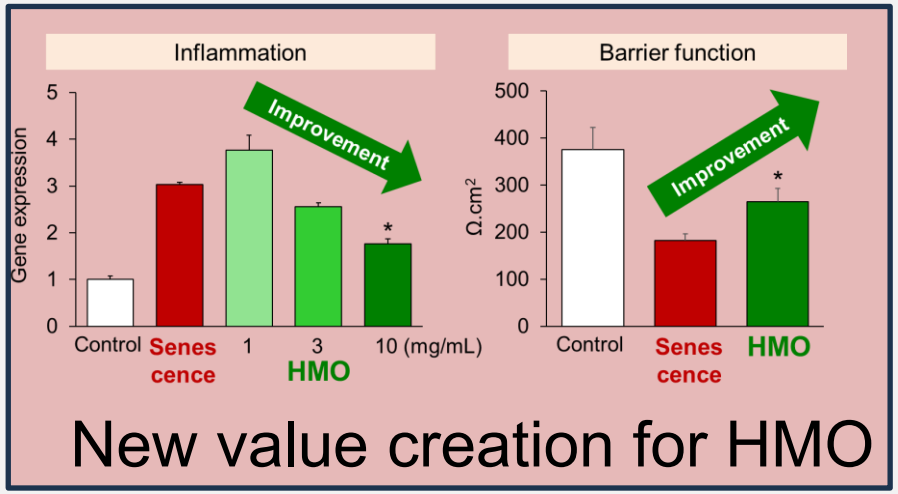


Existing solutions

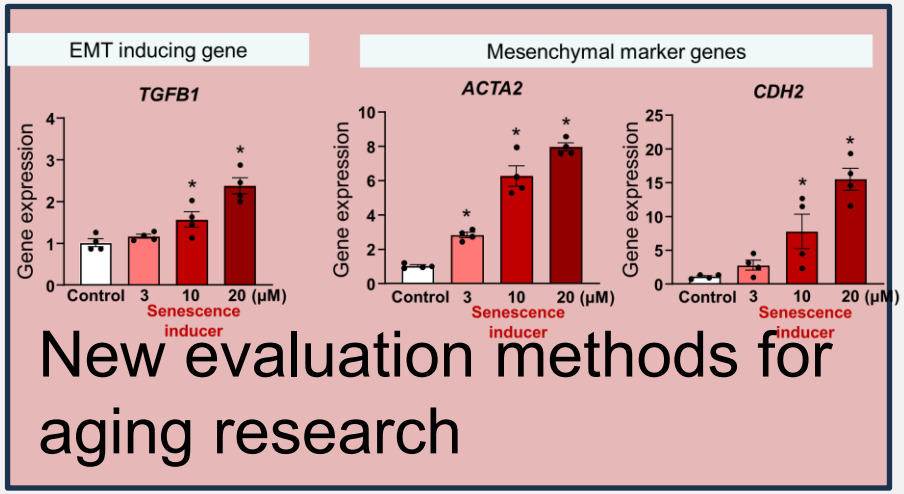
Organoid technology reveals new, testable ways to protect and restore gut function

These discoveries have clear potential to contribute to a very large gut-care market





New value creation for HMO



New evaluation methods for aging research