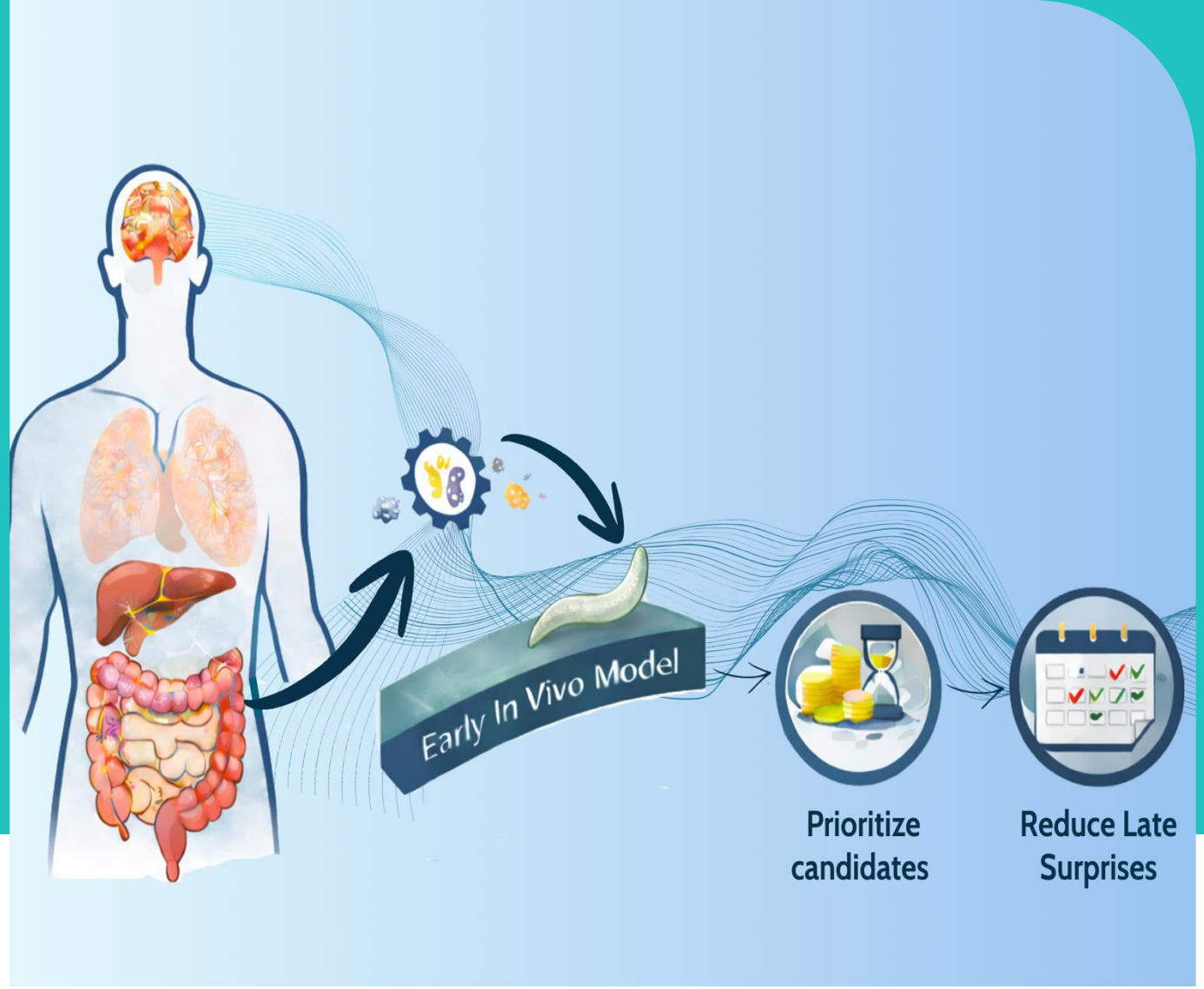
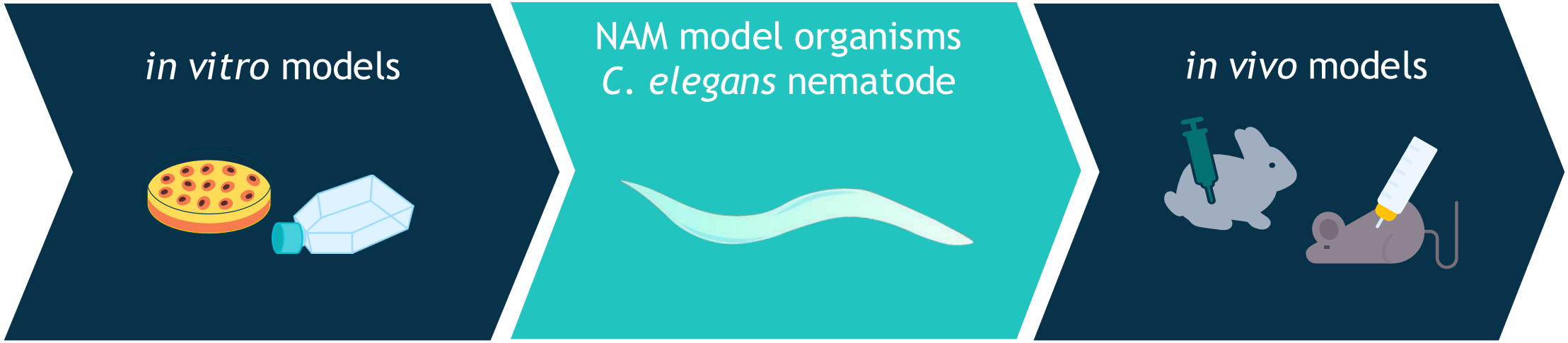
nagi bioscience

De-risking gut-brain projects with an early *in vivo* model



C. elegans is an early *in vivo* decision model.



In vitro models lack a systemic neuroendocrine feedback loop.

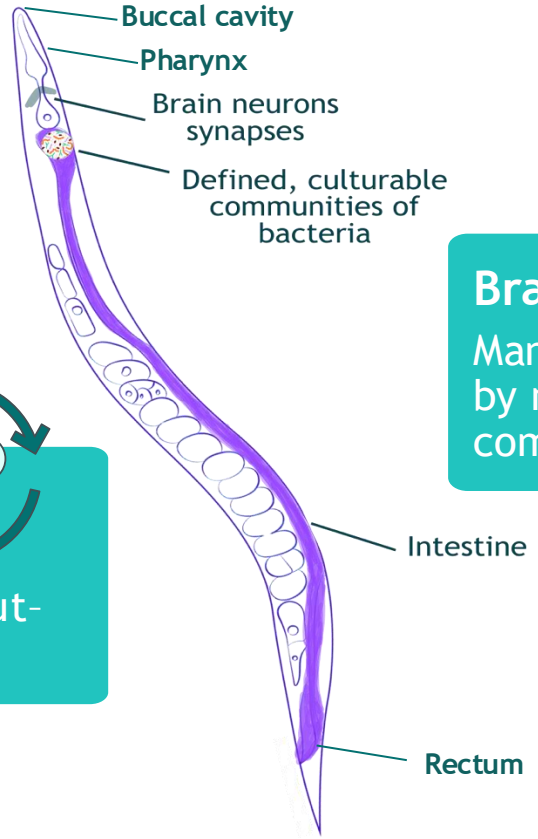
***C.elegans* can bridge this gap by enabling prioritization.**

Microbiome studies are often associative, not elusive in causal inferences (Walter et al., *Cell*, 2020).

Applications of *C.elegans* in gut-brain projects

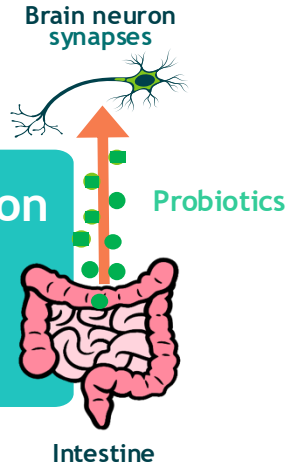
Longevity & Nutrition

Accelerate early discovery pipelines in longevity research.



Brain Function & Neuroprotection

Manage brain chemistry balance by modulating gut microbiota composition.

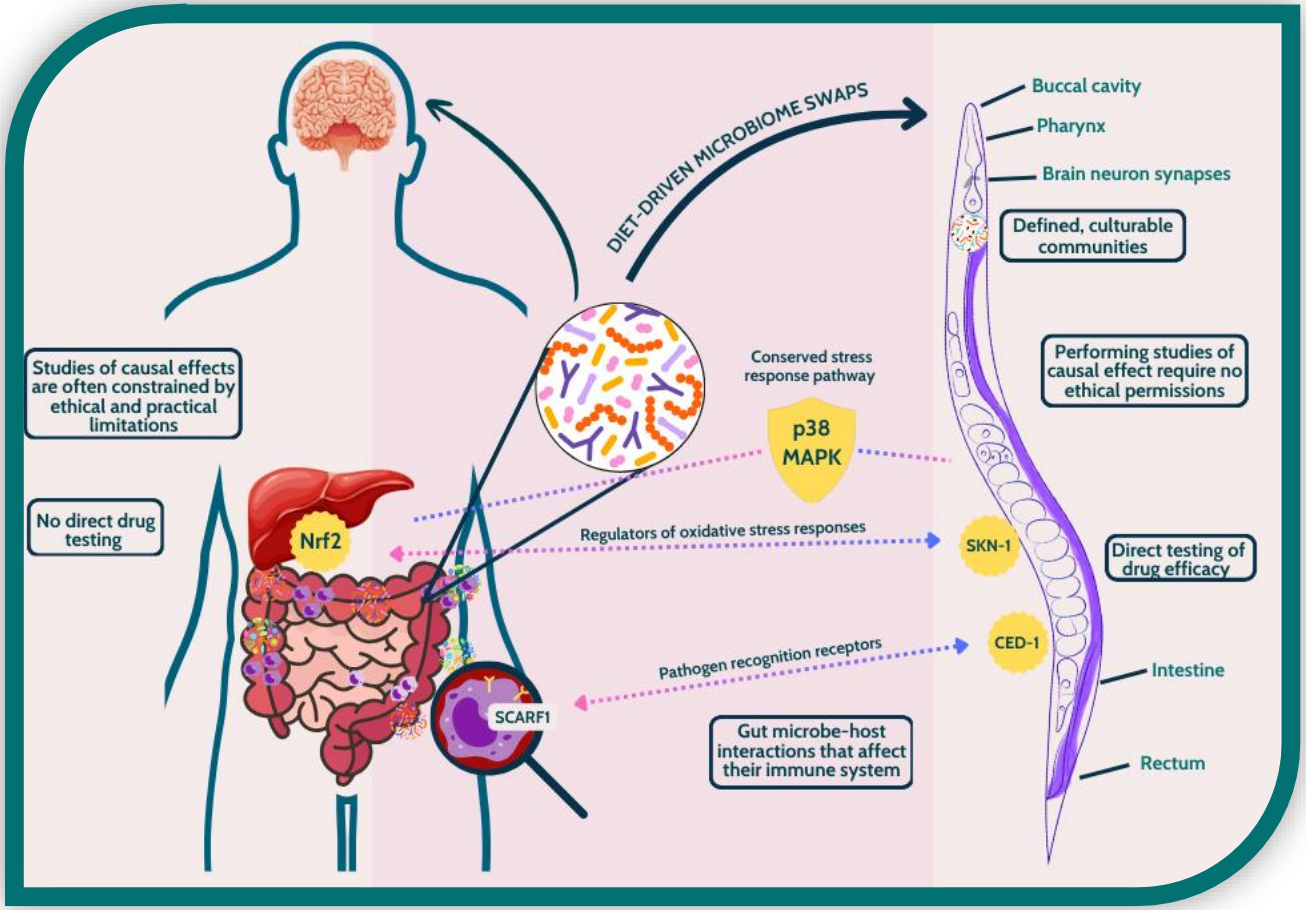


Metabolism & Weight Management

Enable mechanistic investigation of gut-brain interactions.

C. elegans **can produce measurable outcomes, including longevity, neurofunctional phenotypes, and metabolic shifts influenced by the gut-brain axis.**

C.elegans works as *a* translational window into the gut-brain axis



Conserved mechanisms

- Polarized intestinal epithelium with microvilli that performs core digestive/absorptive and barrier functions (1).
- Key epithelial junction/barrier machinery (AJM-1) (2).
- Metabolic, stress-response, and neuroendocrine communication (1).
- Host pathways (FOXO/daf-16, NRF2/SKN-1, p38 MAPK) (see image).

Limitations

- No adaptive immune system.
- No complex human-like microbiome (*C.elegans* can be colonized with defined strains → causality).
- Different anatomy and physiology (pharmacokinetics can not be evaluated).

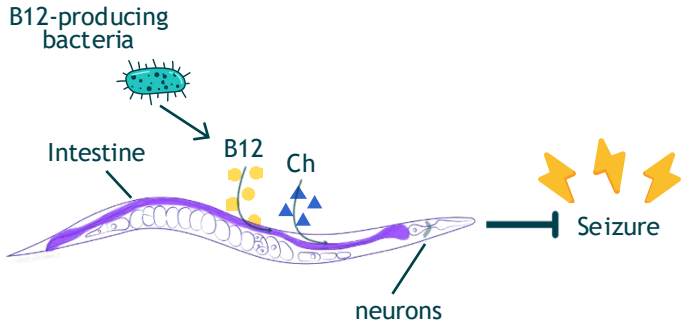
Demostrating causal gut-brain signaling in *C.elegans*

Vitamin B12 produced by gut bacteria modulates neurons' signaling & behavior

WK Kang et al., *Nature Cell* Biology, 2024

▲ Choline: A Compound found in various foods

- Used in a B12-dependent cycle to metabolize fat in the liver
- Used by the nervous system



B12

Choline is used to metabolize fat in the liver

Choline is used by the nervous system

Brain chemical balance

Prevents seizure

B12 deficiency is linked to **schizophrenia, depression, and migraines,** all involving brain chemical imbalance. (P Sahu et al., *NIC*, 2022)

Gut-derived molecule/ ingestion

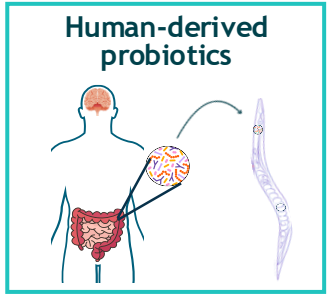
Gut processing/ neuronal function

Systemic effect

Direct causality

Applications of *C.elegans* in gut-brain projects supported by peer-reviewed studies

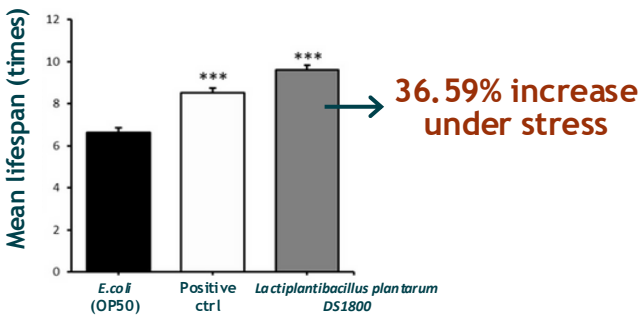
- Nutrition/Supplements
- Metabolism/Weight Managements
- Neuroprotection



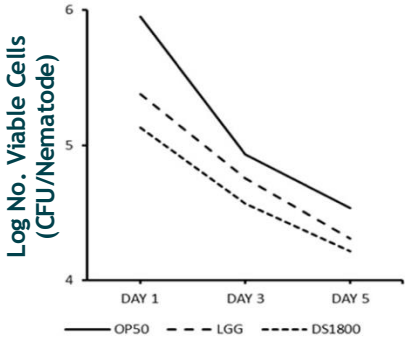
Identifies probiotics that act via host gut signaling rather than microbiome complexity, enabling early prioritization of strains.

Potential probiotic *Lactiplantibacillus plantarum* DS1800 extends lifespan and enhances stress resistance

Upon pathogen infection:



36.59% increase under stress



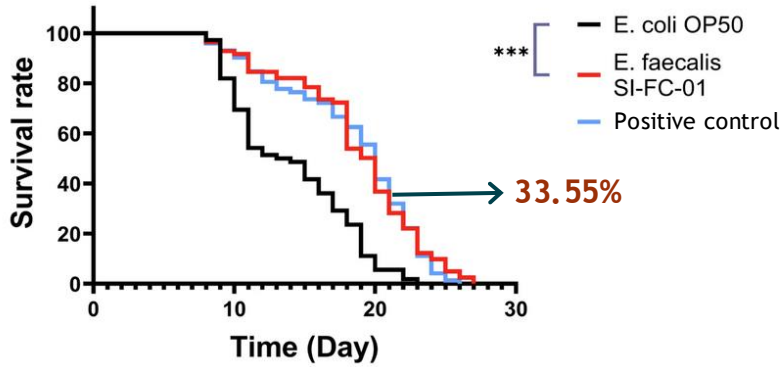
DS1800 consumption led to:

- Increased mean lifespan under stress.
- Decreased pathogen adhesion (*S. Enterica*).

Antimicrobial effect exertion regulated via p38 pathway

S Kim et al., *Frontiers in Physiology*, 2024

Probiotic *Enterococcus faecalis SI-FC-01* enhances the healthspan



33.55%

SI-FC-01 enhanced:

- Lifespan
- Motor ability
- Memory
- Learning Ability

Lifespan & Healthspan extension by modulating DAF-16/FOXO signaling

Y Wu et al., *Nature Scientific Reports*, 2025

Metabolism/Weight Managements

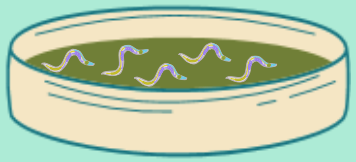
Prioritize strains with causal *in vivo* metabolic efficacy before progression to mammalian models.

L. rhamnosus HA-114

Patent-pending strain to support weight management efforts

An industry example of *C. elegans* as an early *in vivo* screening model for probiotic development

From *C.elegans*



Preclinical studies

Reduction of fat accumulation

Causal *in vivo* efficacy + mechanism

Mice Models

Preclinical studies

Potential psychobiotic action

Obesity models/ Psychobiotic studies

To Humans

LALLEMAND

LALLEMAND HEALTH SOLUTIONS

Double-blind clinical trial

- Mental health
- Eating behavior
- Food cravings
- Insulin levels & resistance
- LDL cholesterol
- Triglyceride levels

Improvement

Targeted clinical endpoints

Neuroprotection

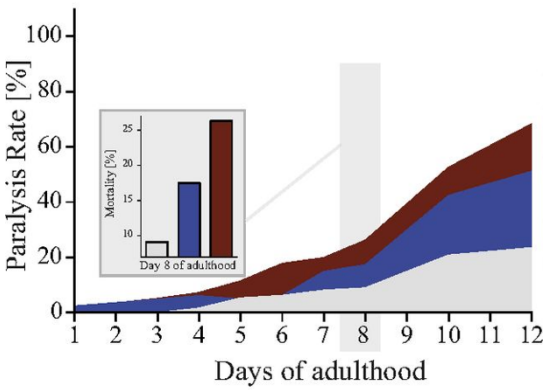
ENT-01 (squalamine): an antimicrobial aminosterol originally originating in the dogfish shark, acts on nerve cells to prevent the unfolded protein response. This small molecule is now prepared synthetically.

Enables early identification of gut-mediated neuroactive compounds and de-risks progression toward advanced disease models.

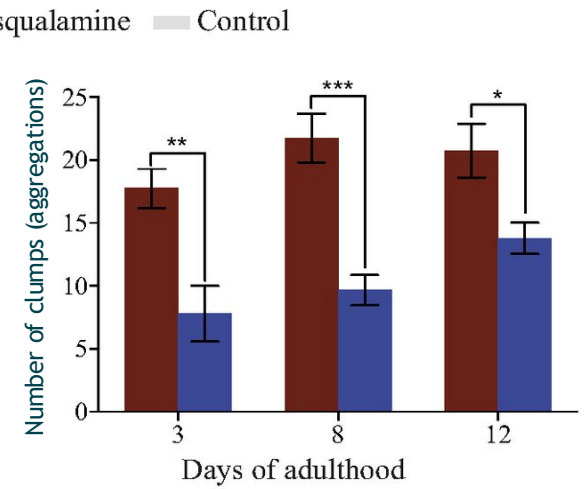
C.elegans research

ENT-01 (squalamine) reduces aggregation and related paralysis in a *C. elegans* model of PD.

Decreased paralysis



Decreased aggregation



Human Insights

Oral ENT-01 targets enteric neurons to treat constipation in PD

Dose-dependent improvement

- in constipation,
- circadian rhythm and sleep,

Significant Improvement

- hallucinations,
- dementia,
- depression
- motor symptoms

More small molecules, like Claramine are now being investigated in PD *C.elegans* model

Samuel T. Dada et al., *Nature communications*, 2024

Accelerate your research with Nagi Bioscience

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In vivo testing at the *in vitro* scale