nagi bioscience

CASE STUDY

A high-glucose *C. elegans* assay

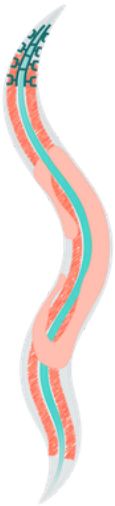
Rapid *in vivo* screening of interventions targeting metabolic health and weight management

Nutrition plays an essential role in overall health, as a well-balanced diet ensures the intake of essential nutrients needed for adequate energy generation and vital processes, such as growth, development, reproduction, movement, and longevity. However, the rapid development of food production and the globalization of food supply have significantly altered dietary patterns, contributing to metabolic dysfunction and related health disorders. Part of the food surplus includes high-sugar diets, which are widely associated with metabolic dysfunction and reduced healthspan (1).

Therefore, nutraceutical developers need faster *in vivo* evidence to prioritize ingredients for metabolic health, weight management, and resilience under nutrient excess before committing to slower and more expensive mammalian studies.

C. elegans: a favorable model in pioneering nutrition science

As a leading model in aging research, *C. elegans* has been extensively used to study lifespan and healthspan, both of which can be regulated by dietary manipulation. This can be explained by the conserved nutrient-sensing metabolic pathways, including insulin/IGF signaling and lipid metabolism (1). For example, in *C. elegans,* excess glucose has been shown to produce a quantifiable decline in lifespan and physiological function, including altered reproduction, increased oxidative stress, and disrupted lipid metabolism (2 & 3). Additionally, as a bacterivorous organism, *C. elegans'* physiology is directly influenced by bacterial composition and metabolism, which facilitates the investigation of host-microbiome interactions. By combining conserved **signaling pathways involved in nutrient-sensing biochemical processes with intrinsic host-microbe interactions, this nematode serves as a promising tool for testing the impact of functional foods and ingredients on metabolic health, stress-induced phenotypes, and longevity.**



A nutritional model

C. elegans shares highly conserved nutrient-sensing pathways with mammals, including insulin/IGF-1 signaling, AMPK, mTOR, and FOXO-mediated stress responses, which regulate energy balance, metabolism, and aging.

Assay relevance

High-glucose feeding in *C. elegans* induces conserved metabolic stress and aging phenotypes that are directionally relevant to obesogenic / Western-diet biology.

Tractable host–microbiome interactions

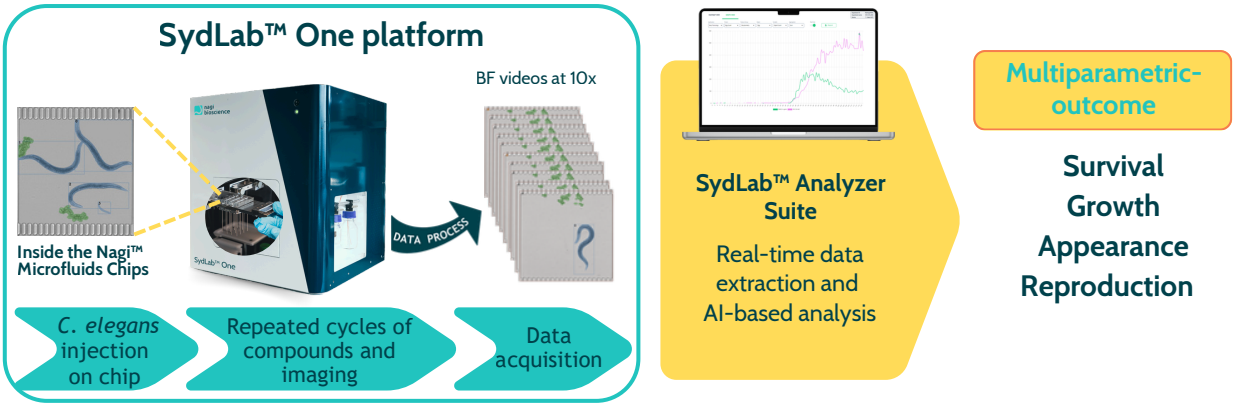
C. elegans feeds on bacteria, allowing precise control of the microbial environment and straightforward manipulation of host–microbe interactions.

Applications

- Screen interventions for metabolic health and weight management.
- Capture microbiome-dependent effects.

High-glucose *C. elegans* assay

Using the Sydlab™ One platform, we developed a streamlined liquid-format assay that captures a coherent glucose-response phenotype across multiple parameters, including **survival**, **reproductive output**, **censoring-associated pathology**, and **physiology-linked readouts** in a single workflow.



Study design

Wild-type worms were exposed to 2% glucose to induce a metabolic-stress phenotype, with 2% sorbitol serving as an osmotic control, enabling the discrimination of glucose-specific metabolic effects from osmotic stress (4). Additionally, worms were fed either live bacteria (OP50) or paraformaldehyde (PFA)-inactivated bacteria under each condition, allowing the evaluation of glucose-specific effects while accounting for potential differences related to bacteria feeding.

Results

The results show that glucose exposure induces a robust **adverse phenotype, including reduced survival and reproductive output, pathology-associated censoring (internal hatching), and a growth and lipid accumulation trend aligned with the literature.**

Reduced survival and lower RMST

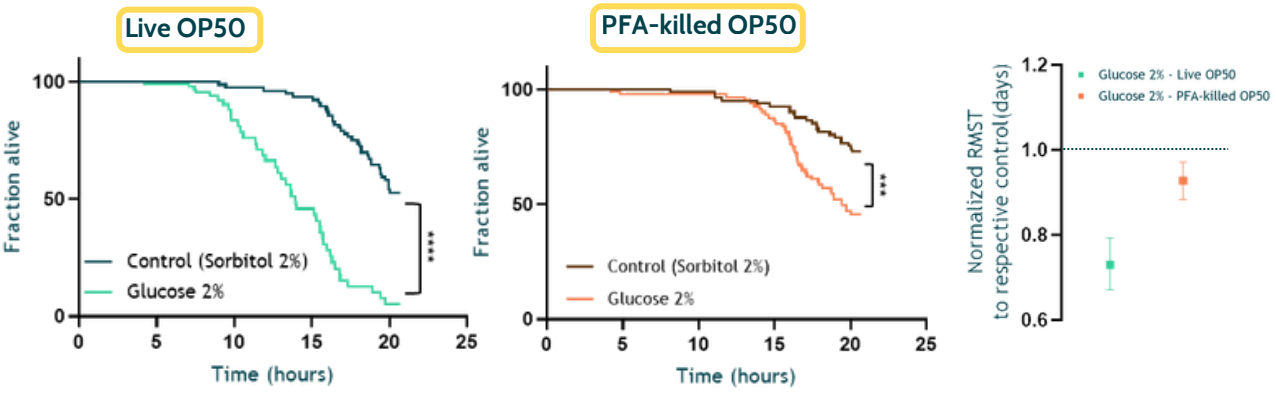
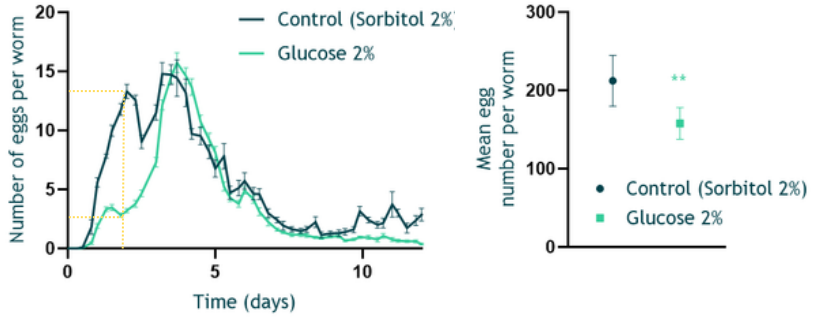


Figure 1. Survival analyses were performed using the Kaplan-Meier method. Survival was quantified using the restricted mean survival time (RMST), expressed in days, which corresponds to the area under the survival curve up to the defined time point. Statistical comparisons were performed using log-rank test ***p<0.001; **** p<0.0001.

Reduced and delayed reproduction capacity

Live OP50

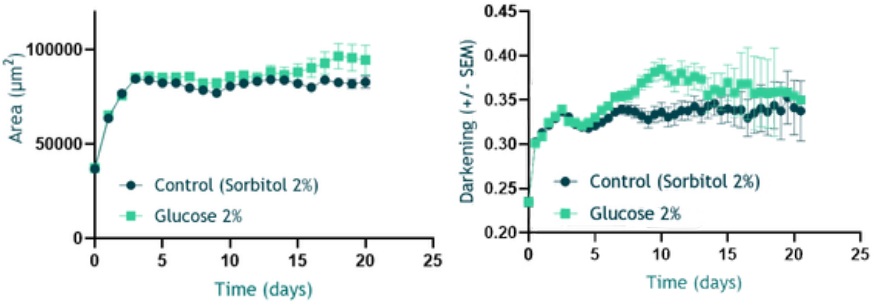


In high-sugar diets, reproductive output is often reduced, indicating **an impaired physiological function and disrupted energy allocation**.

Figure 2. Reproduction was assessed by the time-course of egg-laying in worms fed with live OP50 and expressed as the mean number of eggs per worm. Statistical comparisons were performed using Welch's t-test. $p<0.05$, **

A growth & lipid accumulation trend

Live OP50



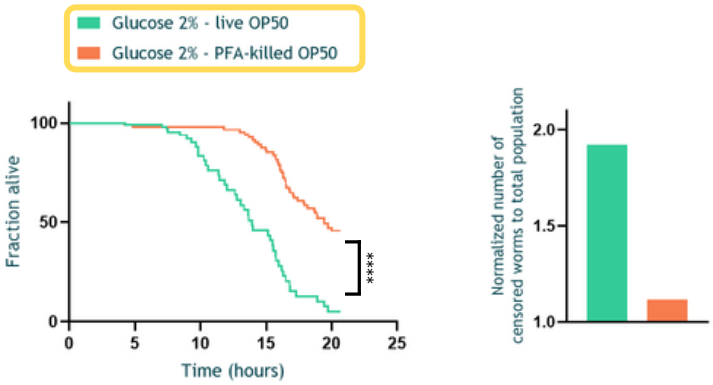
Broader physiology-linked changes, including increased growth and lipid accumulation (darkening), can be induced upon high-glucose diets (4) **consistent with disrupted energy homeostasis and impaired organismal function.**

Figure 3. Nutrient signaling and lipid accumulation were assessed by the time course of worm area (µm²) and darkening, respectively, in the worms fed live OP50 and treated with 2% glucose or sorbitol. Darkening in worms often corresponds to increased lipid accumulation (lipid droplets) and reflects metabolic overload.

Bacterial metabolic activity contributes to the severity of glucose-induced dysfunction in *C. elegans*

A stronger phenotype is observed with live OP50 compared with PFA-killed OP50, suggesting that bacterial metabolism is a major contributor to glucose-induced stress. This interpretation is supported by Kingsley et al. (2021), who showed that bacterial processing of glucose reduces worm lifespan and healthspan, including locomotion and oxidative-stress resistance, even in an experimental design where the worms themselves do not directly contact the added glucose. **The results below focus on the differences between the populations fed live OP50 and PFA-killed OP50 on survival and physiological stress, indicated by the internal hatching, providing insights into the role of bacterial metabolic activity in host glucose stress.**

Survival & Pathology-associated censoring



High-glucose diets have also been reported to increase egg retention with internal hatching (4), **a biologically relevant pathological indicator of reproductive and physiological stress.**

Figure 4. Survival analyses were performed using the Kaplan-Meier method. Censored worms in survival assays include internal hatching (bagging), in which embryos hatch within the worms, causing death. The fraction of censored worms was normalized to the total population. Statistical comparisons were performed using the log-rank test. **** $p < 0.0001$.

This assay captures how microbial activity shapes the host response to excess dietary glucose, providing a whole-organism platform to screen interventions that restore function under microbiome-dependent metabolic stress.

This study establishes a high-glucose *C. elegans* assay as a robust and scalable platform to model diet-induced metabolic stress and evaluate intervention efficacy at the whole-organism level. By combining survival, reproductive output, growth, and lipid-associated phenotypes, the assay captures multiple dimensions of organismal health. Importantly, the observed modulation by bacterial state highlights the contribution of host–microbe interactions, providing additional mechanistic insight. Together, this framework enables rapid screening of ingredients that improve metabolic resilience and functional health.

References:
1. Zhu G et al., *J. Integr. Biol. (Camb)*. 2015
2. Kingsley SF et al., *Sci Rep.*, 2021
3. Alcántar-Fernández et al., *PLoS One*, 2018
4. Lee SJ et al., *Cell Metab*. 2009
5. Wang, Y., et al., Critical Reviews in Food Science and Nutrition, 2024

All bioactivities of dietary nutrients studied using *C. elegans*

Carbohydrates:
Glucose, Fructose, Sucrose, Oligosaccharides, Polysaccharides

Lipids & fatty acids:
Linoleic and linolenic acids, Oleic, arachidonic, eicosapentaenoic, and docosahexaenoic acids

Proteins, Vitamins & Minerals
B12, C, D, E, Folate, Zinc, Iron, Calcium, Selenium
(5)

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info@nagibio.ch