Accelerating probiotic screening: Insights into gut health using *C. elegans* model

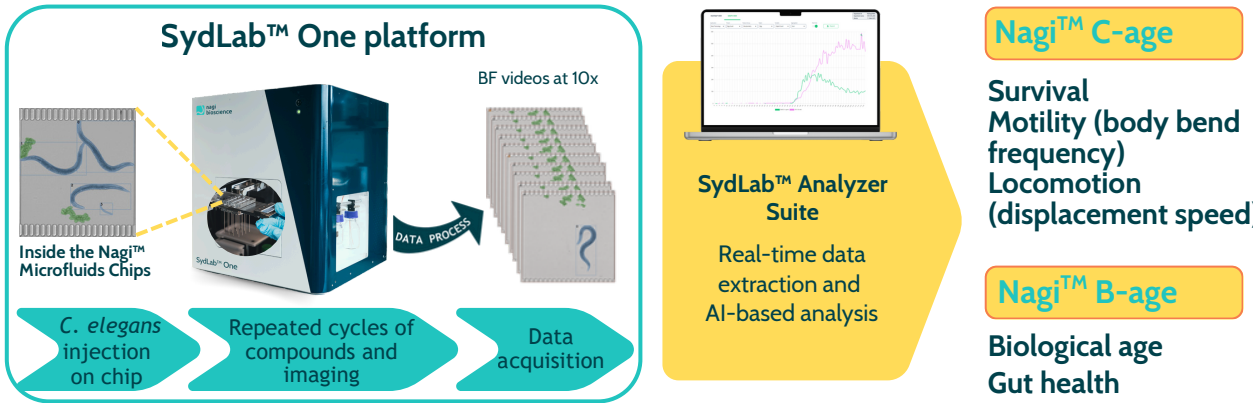
How Nagi Bioscience delivered key *in vivo* findings for DTU Novo Nordisk Foundation Center

The Novo Nordisk Foundation Center for Biosustainability (DTU Biosustain) develops methods and technologies for large-scale production of natural products, sustainable foods, and sustainable biochemicals. Using our proprietary **SydLab™ One platform,** DTU accelerated the screening of several candidates, unraveling valuable insights into their potential applications for gut health and longevity. Here, we share findings on *Saccharomyces boulardii,* a probiotic yeast widely used for its beneficial effects on gut health. Emerging evidence suggests that *S. boulardii* can function as an anti-aging intervention by modulating intestinal flora (1) and intestinal barrier integrity (2).

Why is *C. elegans* a powerful model to study probiotics and gut health?

C. elegans serves as an exceptional *in vivo* model to explore the interplay between probiotics and host physiology. Its well-characterized gut and nervous systems, together with conserved molecular pathways, allow researchers to uncover how microbial metabolites influence healthy aging, metabolism, and overall organismal function. Probiotic interventions in *C. elegans* have demonstrated effects on longevity (3), lipid homeostasis (4), stress resilience (5), and even protein homeostasis (6), mechanisms that are directly relevant to human gut-brain and gut-metabolic health. This makes *C. elegans* a highly predictive and efficient system for screening probiotic candidates and elucidating their mechanisms of action before advancing to mammalian or clinical studies.

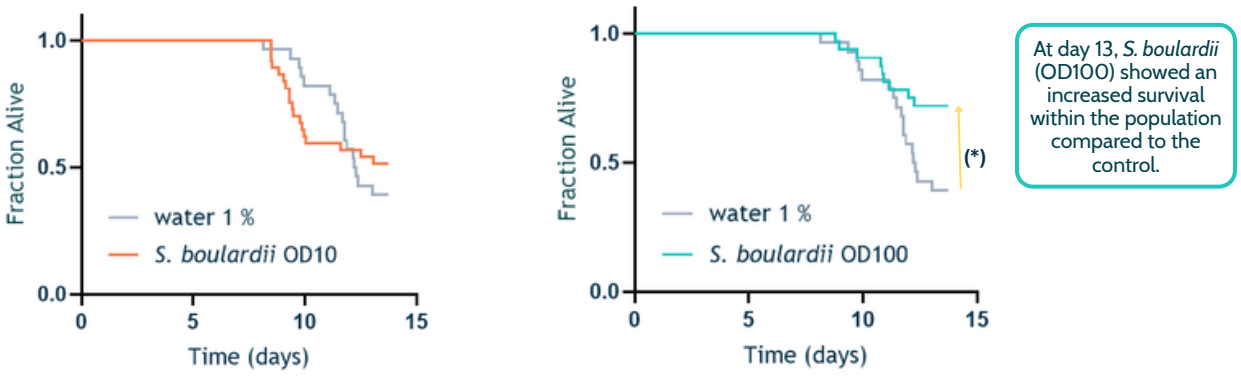
Dual approach: SydLab™ One platform + Nagi™ B-Age



Results

The nematodes were maintained on inactivated, dried OP50 as a carrier diet and received *Saccharomyces boulardii* in different preparations: inactivated cells with culture supernatant, then separated inactivated yeast cells, and cell-free supernatant, at two different concentrations (OD10 & OD100). The results below focus on healthspan and gut health, **revealing that *S. boulardii* improved mobility and biological age in a dose-dependent manner. Improved mobility (motility & locomotion) reflects preserved neuromuscular and metabolic function, indicating a beneficial impact on overall healthspan.**

Increased early-life survival



At day 13, *S. boulardii* (OD100) showed an increased survival within the population compared to the control.

Figure 1. Survival curves of *C. elegans* populations with two different doses of *S. boulardii* over 13 days. Survival analyses were performed using the Kaplan-Meier method, and statistical significance between survival curves was calculated using the log-rank test. Significant difference (p>0.05) is indicated by an asterisk (*).

Improved Motility

Dose-dependent effect on body bending frequency

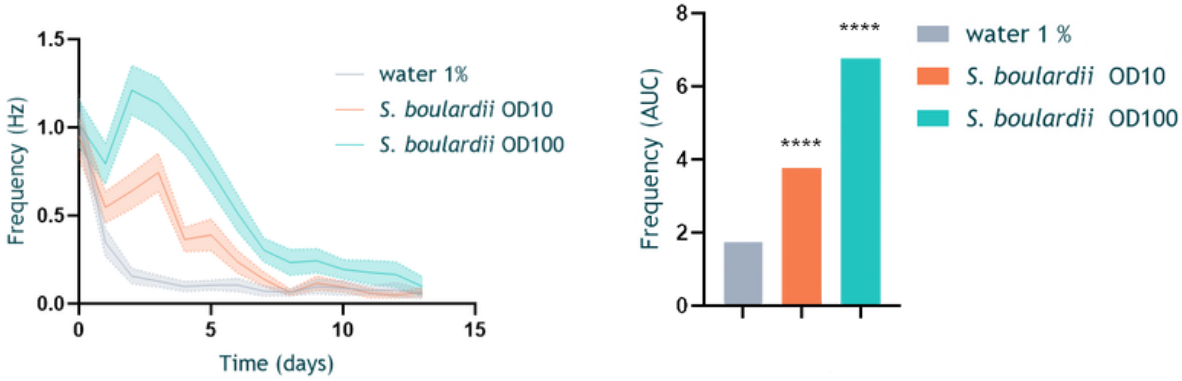


Figure 2. Body bending frequency was measured longitudinally. Statistical analysis was performed using two-way ANOVA to assess overall differences across curves, followed by Bonferroni's multiple comparisons test. Significant differences (p>0.0001) are indicated by asterisks (****).

Improved Locomotion

Dose-dependent effect on displacement speed

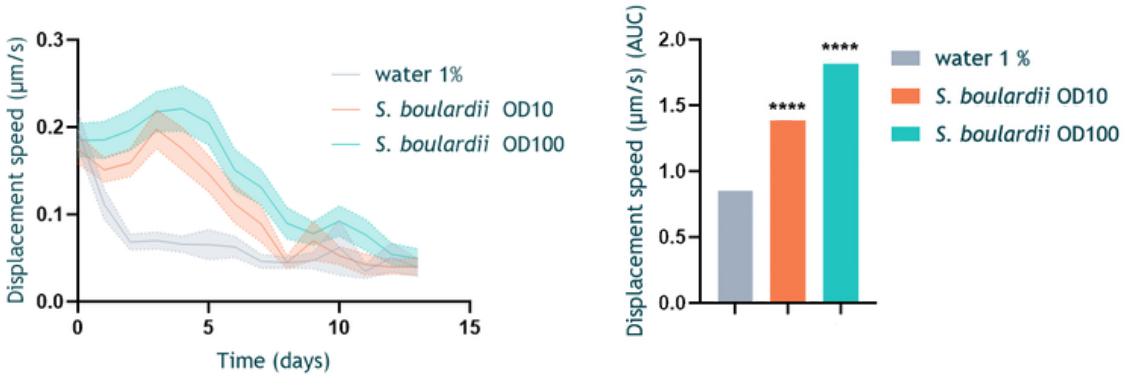


Figure 3. Locomotion was measured longitudinally. Statistical analysis was performed using two-way ANOVA to assess overall differences across curves, followed by Bonferroni's multiple comparisons test. Significant differences (p>0.0001) are indicated by asterisks (****).

Dose-dependent improvement of the biological age

To further investigate the impact of *S. boulardii* on healthspan, DTU leveraged Nagi™ B-Age, the phenotypic clock, which allowed them to quantify the biological age of *C. elegans* and identify trait-specific improvements such as intestinal health. Intestinal health is evaluated through multiple morphological parameters, including gut atrophy (the ratio of intestinal area to total body area), pigmentation, and tissue texture. Since *S. boulardii* at OD 100 showed a clear positive effect on intestinal integrity at day 10, the Nagi™ B-Age analysis was extended to separated postbiotics (inactivated yeast cells) and parabiotics (the supernatant alone).
This design enabled DTU to distinguish whether the observed benefits originated from a cooperative mechanism or were driven primarily by structural cell components or soluble metabolites.

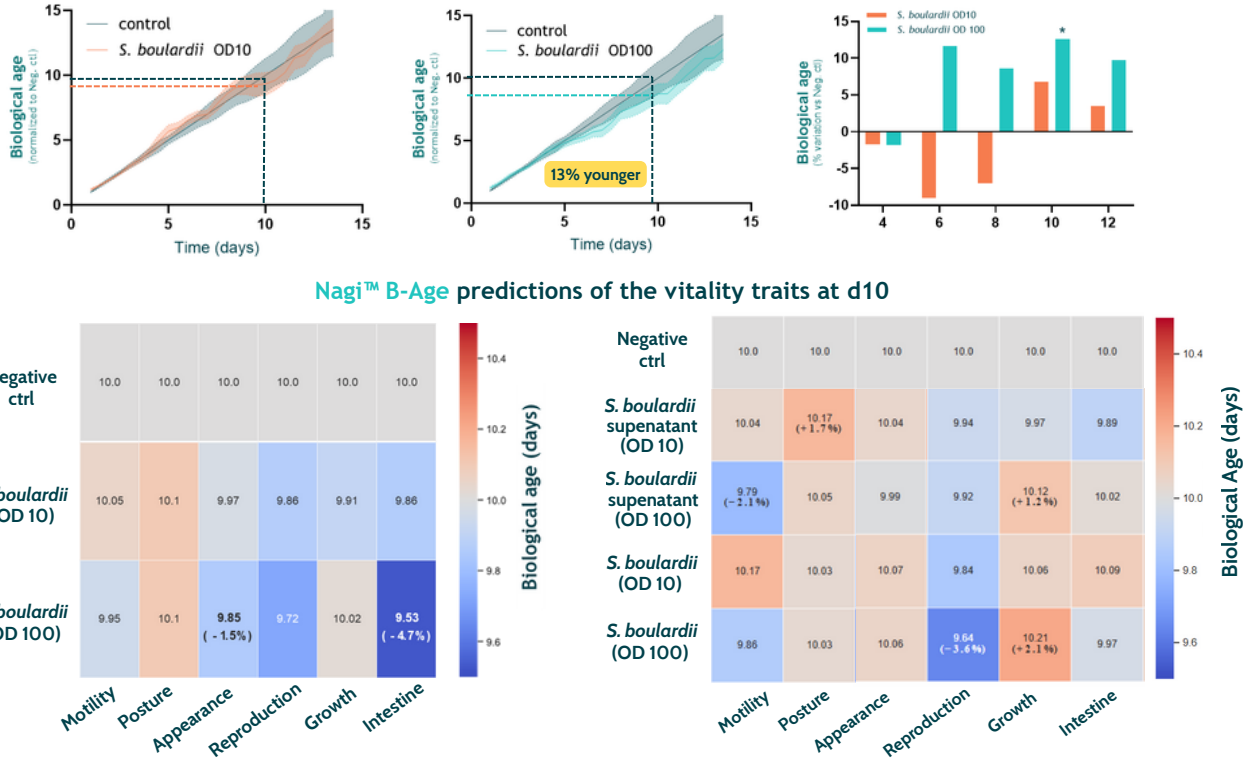


Figure 5: Evaluation of *S. boulardii* impact on *C. elegans* healthspan using Nagi™ B-Age. Biological age prediction by Nagi™ B-Age, from day 0 to 12, for *S. boulardii* at OD10 & OD100. A barplot illustrates the variation in predicted biological age compared to the control at different time points. Statistical significance was assessed with two-way ANOVA followed by Bonferroni's multiple comparisons test. * p<0.05. The Nagi™ B-Age prediction was further decomposed into individual vital traits. Significant changes in biological age, relative to the negative control, are expressed as percentage improvements or deteriorations. The overall change in biological age reflects the cumulative effect of changes across all vital traits.

Since neither the cell fraction nor the cell-free supernatant alone produced a significant change in intestinal biological age, the observed improvement seems to require the co-presence of cell-associated structures and soluble components. This would be consistent with a cooperative mechanism in which cell walls act as a delivery system for bioactive metabolites and/or enable concurrent receptor engagement at the intestinal epithelium.

Ready to test your probiotics?

1. (Gopalan et al., *Cureus*, 2023)
2. (Terciolo et al., *Clinical and Experimental Gastroenterology*, 2019:12 67-82, 2023)
3. (Y Wu et al., *Nature Scientific Reports*, 2025)
4. (Labarre et al., *Communications Biology*, 2022)
5. (Kim et al., Frontiers in Physiology, 2024)
6. (Walker et al., *PLOS Pathogens*, 2021)