

#### **APPLICATION NOTE**

Early *in vivo* insights for therapeutic discovery in neurodegeneration Early *in vivo* insights for therapeutic discovery in <u>neurodegeneration</u>



Neurodegeneration research seeks to understand the mechanisms behind the progressive loss of neuronal structure and function, which underpins debilitating conditions such as Alzheimer's, Parkinson's, ALS', and Huntington's diseases. As the prevalence of these disorders increases with aging populations, the demand for efficient, reliable, and scalable *in vivo* research tools is more pressing than ever.

Nagi Bioscience provides an innovative solution tailored to the neurodegeneration field, enabling researchers to gain real-time, actionable insights into the effects of diverse interventions on neuronal health.

With its ethical, scalable platform, Nagi Bioscience streamlines the evaluation of potential therapeutic compounds, accelerating breakthroughs that can mitigate neurodegenerative decline and improve the quality of life for those affected by these challenging conditions.

#### Achieve the otherwise unattainable

Automated, *in vivo* at *in vitro* scale: Nagi's system uniquely combines the benefits of *in vivo* testing with the efficiency and scale approximating *in vitro* setups. This approach enables rapid, scalable studies, minimizing the need for vertebrate models and associated ethical concerns.

**Precise quantification of neuronal decline using fluorescent bio-markers:** Accelerates decisionmaking, enabling the distinction between drug mechanisms of action and the detection of subtle physiological changes often missed by traditional endpoint assays. Leverage systemic analysis to simultaneously measure healthspan.

**Cost-effective preclinical solutions:** Leverage the *C. elegans* model to obtain translationally relevant *in vivo* results earlier in the therapeutic development process, bridging the gap between *in vitro* systems and costly vertebrate models. Conduct low-cost, ethically sound preclinical studies and aim for publication-ready data.

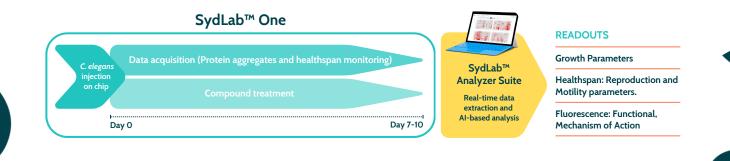
	in vitro	nagi bioscience	Mice
Functional screening using fluo-bio- markers and healthspan analysis.	> 384 drugs/month	From 192 to 274 drugs/month	3-5 drugs/month
Translational value	Low	High	High

The numbers of drugs per month/year refer to the number of compounds that can be tested in 30 days, without technical repetitions or controls.



#### From research to results: Our approach

Age synchronized populations of *C. elegans* are injected into the microfluidic chips and controlled by a fully automated protocol. In each channels, *C. elegans* are exposed to a well-defined liquid environment, including the compounds to be tested. All readouts are monitored all along their life cycle. In addition to neurodegeneration-related insights, the high-content imaging enables the analysis of diverse phenotypes, supporting broader applications.

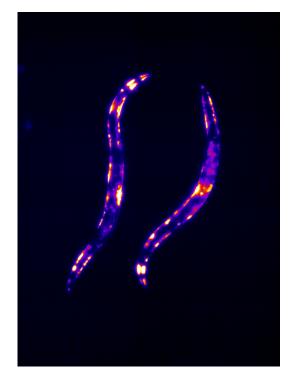


#### C. elegans: A gateaway to studying neurodegeneration

*Caenorhabditis elegans* has become a powerful ally in the quest to slow aging and extend the healthy years of human life. With its short lifespan and genetic similarities to humans, *C. elegans* allows researchers to rapidly study how different interventions can protect against neurodegeneration.

This model enables scientists to explore the biological roots of neuronal decline, and to pinpoint compounds and genetic pathways that delay neuron deterioration. As a whole organism, *C. elegans* offers a more relevant and integrated system for studying neurodegeneration compared to cell cultures or organoids, while still avoiding the ethical concerns, high costs, and logistical limitations of vertebrate models.

Discoveries made with *C. elegans* provide valuable insights that help guide the development of therapies aimed at improve the patient's quality of life.



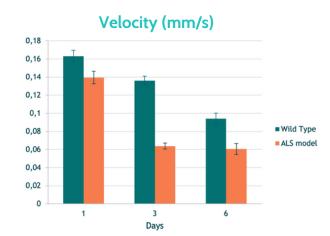
YFP-tagged SOD1 in the ALS C. elegans model (day 6 on SydLab  $^{\rm TM}$  One).

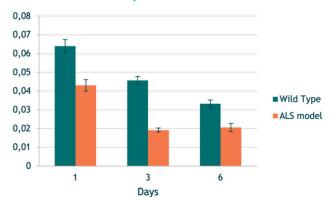
# Advancing neurodegeneration research with SydLab™ One

#### Introduction

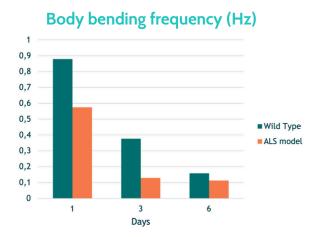
In the following case study, we used Nagi Bioscience's fully automated solution, to showcase how SydLab<sup>™</sup> One platform enables efficient visualization and quantification of neurodegeneration progression in *C. elegans* model for ALS' disease.

We first assessed the motility of the ALS' model, additionally, we monitored and quantified SOD1-YFP protein levels associated with ALS progression.





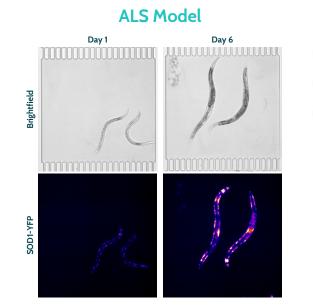
Head amplitude (mm)



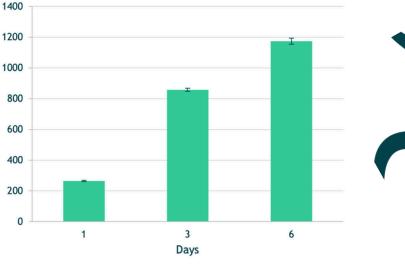
The SydLab<sup>™</sup> One platform captures the age-related decline in motility (a readout of healthspan) in both WT and ALS models, with the ALS' model exhibiting significantly lower motility compared to WT up to day 6.

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Additionally, the SydLab<sup>™</sup> One platform enables the visualization and quantification of YFP-tagged SOD1 in the ALS' model. From day 1 to day 6, it detects a marked increase of protein aggregates, measures using the total fluorescence intensity.



#### Protein aggregate intensity (AU)



#### Conclusion



The SydLab<sup>™</sup> One platform effectively quantified the progression of neuronal decline by monitoring the aggregation dynamics of the SOD1-YFP protein, providing detailed insights into disease progression at a cellular level.



Furthermore, by also measuring motility data, SydLab<sup>™</sup> One enabled simultaneous assessment of healthspan, offering a comprehensive view of the age-related decline in both wild-type and ALS models.

This case study highlights how Nagi Bioscience's neurodegeneration solution empowers researchers to obtain reliable, high-quality *in vivo* data more efficiently and with fewer resources than conventional methods. By streamlining complex workflows and reducing the need for manual intervention, the solution offers an affordable and practical option for neurodegeneration studies, ultimately contributing to more informed therapeutic strategies.

# The ultimate solution providing high-throughput, ethical full-organism data

Leveraging the much-vaunted *C. elegans* organism model, SydLab<sup>™</sup> One introduces the revolutionary Organism-on-Chip technology, which combines the power of in vivo assays with the convenience and scalability of in vitro testing. Researchers can now conduct experiments on over 1,000 organisms simultaneously, with results analyzed in real-time through our accompanying AI-driven software suite.

## 1 High reproducibility

SydLab™ One automated workflows and deep-learning analytics ensure robust, user-independent results every time.

## 2 Higher Speed; Lower Cost

SydLab<sup>™</sup> One's Plug-and-Play, chip-based system saves you time and energy during the experiments, as well as reducing cost per assay. SydLab<sup>™</sup> One allows you to do more, for less.





### **Real-Time Data**

SydLab<sup>™</sup> One integrates our advanced AI-driven software suite, empowering real-time experiment monitoring and delivering clear, actionable data analysis.

# **4** No Ethical Concerns

Leveraging the highly validated *C. elegans* as a model organism, SydLab<sup>™</sup> One offers a recognized ethical alternative to vertebrate testing, advancing research with a focus on sustainability and responsibility.





# Explore our technologies and research solutions



Discover the capabilities of SydLab<sup>™</sup> One with the Discovery Pack experience

Let's connect

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