SydLab™ One: An Automated Microfluidic Platform for Scalable, High-Content Toxicological Screening in *C. elegans*

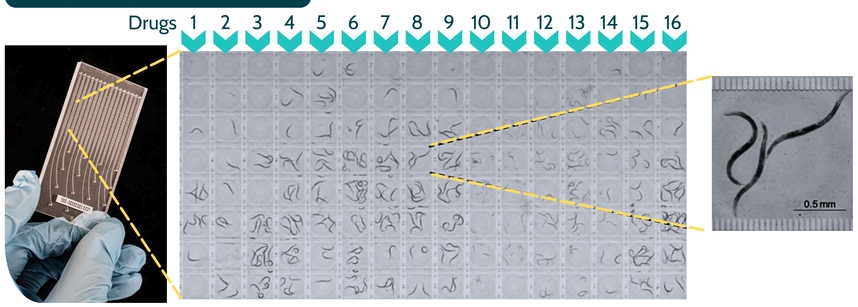
Marie Pierron, Alexnadre Vaudano, Morgane Bourgeois, Lazar Stojkovic, Fabien Tâche, Matteo Cornaglia & Laurent Mouchiroud*
Nagi Bioscience SA, EPFL Innovation Park, Rue des Jordils 1A, CH-1025 St-Sulpice, Switzerland. *email: laurent.mouchiroud@nagibio.ch

Conventional toxicological assays have limitations: cellular models lack organismal complexity, and vertebrate testing is costly, ethically constrained, and low throughput. *Caenorhabditis elegans* provides a promising alternative, enabling whole-organism testing at an *in vitro*-like scale with easier handling and lower costs. To enhance scalability, we developed SydLab™ One, an automated microfluidic platform for culturing, treating, and imaging *C. elegans* populations throughout their lifecycle. Hourly brightfield and fluorescence imaging, combined with machine learning-based analysis, generate multi-phenotypic data for both parental *C. elegans* and progeny. Our High-Content Screening (HCS) approach provides early insights into chemical modes of action, while fluorescence imaging with reporter strains expands phenotypic readouts for mechanistic studies.

We validated SydLab™ One by screening 21 benchmark chemicals at five concentrations each, including 16 known toxicants (e.g., methotrexate, thalidomide) and 5 considered safe (e.g., sodium chloride, ascorbic acid). The platform achieved 85.7% accuracy in classifying chemical profiles and a 93.3% positive predictive value for toxic effects. These results demonstrate its potential for scalable, high-accuracy toxicological and ecotoxicological testing, supporting early dose calibration and hazard identification.

SydLab™ One: Fully automated compounds testing and multi-phenotypic analysis on *C. elegans*

Nagi's Organism-on-Chip



- MWM patented technology: Microfluidic chips relying on passive hydrodynamics.
- 64 fluidic lines = 64 independent experimental conditions (SydLab™ One has a max. capacity for 4 chips in parallel).
- ~1000 organisms in total total

SydLab™ One

- Automated culture and treatment of up to 64 conditions in parallel.
- Programmable acquisitions of BF and fluorescence images and videos.
- Active temperature control in the 10-40°C range.

SydLab™ Analyzer Suite

- User-friendly software to run and mnitor experiments.
- Time-resolved / high-content data extracted using AI
- Integrated statistical analysis and data interpretation algorithms

Drug toxicity and efficacy profiling

Reproductive Toxicity Assay

SydLab™ One

C. elegans injection on chip (L1)

C. elegans confined in microfluidics, constant feeding and image acquisition

ReproTox

Compound treatment (L4 stage)

Hour 0 — Developmental Period — Hour 50 — Reproductive Period — Hour 130

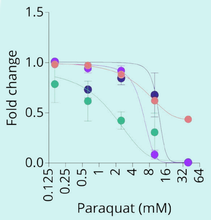
Access to processed images acquired every hour and datasets

SydLab™ Analyzer Suite

Real-time data extraction and AI-based analysis

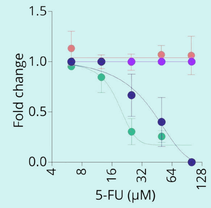
RESULTS 1 - Dose-dependent response to Paraquat and 5-Fluorouracil (5-FU)

A Multi-phenotypic analysis- Paraquat



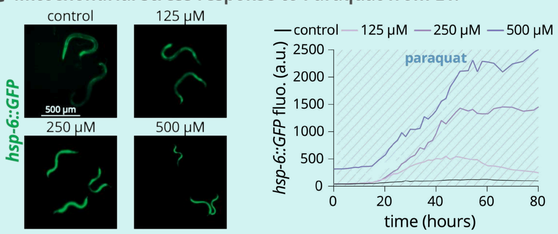
	End points	NOAEL (mM)
Maternal effects	Maximum length	2.5
	Growth dynamic	2.5
Repro toxicity	Fertility	2.5
	Sexual maturity	0.16
	Egg accumulation	0.16
	Embryo survival	0.16
	Larvae emergence	0.16
	Larvae accumulation	0.63

B Multi-phenotypic analysis- 5-FU

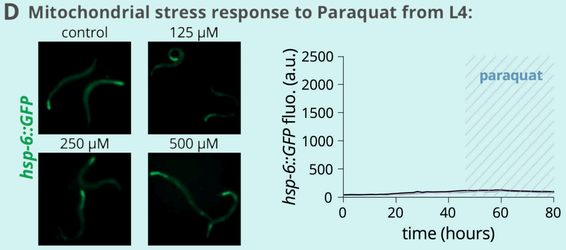


	End points	NOAEL (µM)
Maternal effects	Maximum length	>100
	Growth dynamic	>100
Repro toxicity	Fertility	>100
	Sexual maturity	>100
	Egg accumulation	50
	Embryo survival	50
	Larvae emergence	50
	Larvae accumulation	12.5

C Mitochondrial stress response to Paraquat from L1:



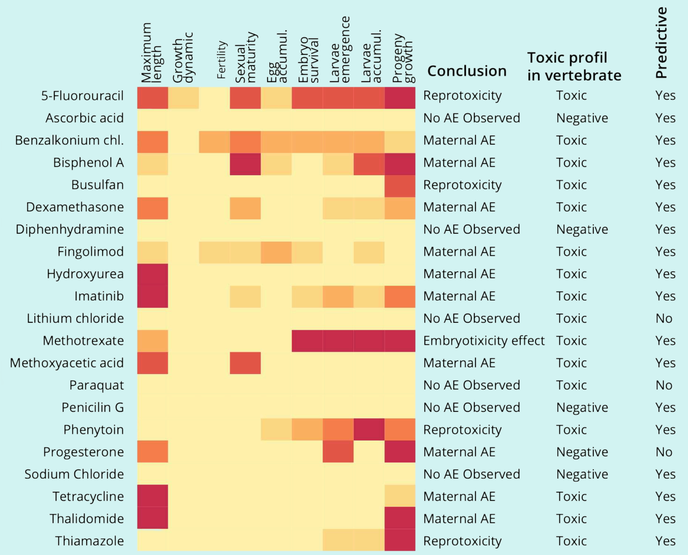
D Mitochondrial stress response to Paraquat from L4:



CONCLUSION

Paraquat induces **major maternal adverse effect (AE)** at high doses (NOAEL: 2.5mM) and **significant reprotoxic effect** at lower doses (NOAEL: 0.16mM). Expression of the mitochondrial stress reporter (hsp-6::GFP) is increased by paraquat treatment at L1 stage but not by the treatment at L4 stage. Therefore, Paraquat induced AE are not correlated with mitochondrial stress response. As reported, 5-FU has no maternal AE at the doses tested but a **strong reprotoxic impact** at mid doses (NOAEL: 50µM).

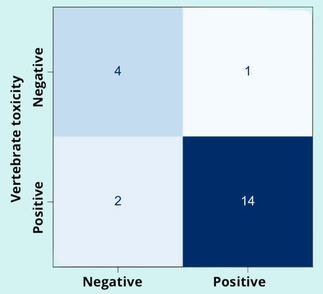
RESULTS 2 - Blind testing of 21 benchmark chemicals



6 concentrations vs solvant (µM):

<12	37	75	111	333	>1000

3 technical replicates per experiment
2 independent experiments



Positive pred. = 93.3%
Negative pred. = 66.7%
Accuracy = 85.7%

Specificity = 80%
Sensitivity = 87.5%

Balanced Accuracy = 83.8%

CONCLUSION

This study highlights the strong advantages of our innovative technology which yield **(1) reproducible and accurate results** thanks to standardized protocols, **(2) an automated dosing of chemicals with low liquid consumption** and **(3) multi-phenotypic readouts in real-time**. SydLab™ One represents the first «all-in-one» *C. elegans* microfluidic lab that contributes to the rapid identification of toxic compounds in the early stages of the drug discovery pipelines.