



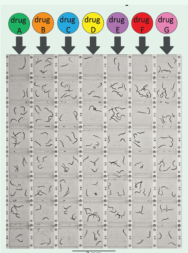
# MICROFLUIDIC-BASED ROBOTIC DEVICE FOR FULLY AUTOMATED HIGH-CONTENT SCREENING ON *C. ELEGANS* AS A NOVEL NAMs PLATFORM FOR CHEMICAL TOXICITY ASSESSMENT

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## SYDLAB™ ONE: FULLY AUTOMATED COMPOUNDS' TESTING AND MULTI-PHENOTYPIC ANALYSIS ON *C. ELEGANS*

### Nagi™ Microfluidic Organism-on-Chip



- Patented microfluidic design, relying on passive hydrodynamics.
- 64 fluidic lines = 64 independent experimental conditions.
- +1000 organisms analyzed simultaneously.

### SydLab™ One Robotic Platform

Automated worms' culture, treatment, and imaging of up to 64 independent conditions in parallel.



- Programmable acquisitions of bright-field and fluorescence images and videos.
- Active temperature control in the 15-38°C range for automated culture.

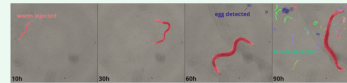
## SYDLAB™ ANALYZER SUITE: REAL-TIME DATA EXTRACTION, ANALYSIS & INTERPRETATION

### Real-time AI-based analysis of +25 data-points/hour/organism

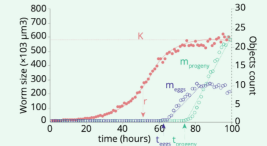


- Time-resolved high-content data extracted using AI.
- Integrated statistical analysis and data interpretation algorithms.

### AI-based object detection



### Automated, real-time and robust analysis



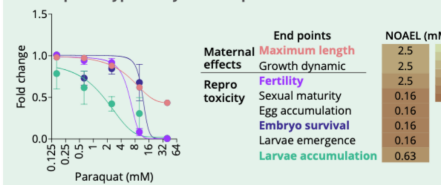
## VALIDATION OF THE REPRODUCTIVE & DEVELOPMENTAL TOXICITY (DART) ASSAY ON THE SYDLAB™ ONE PLATFORM

### BY SYDLAB™ ONE

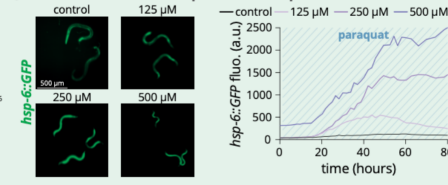


### RESULTS 1 - Dose-dependent response to Paraquat and 5-Fluorouracil (5-FU)

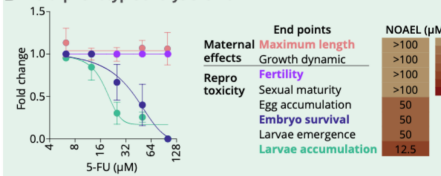
#### A Multi-phenotypic analysis- Paraquat



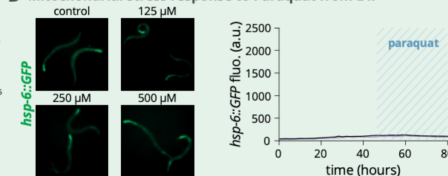
#### C Mitochondrial stress response to Paraquat from L1:



#### B Multi-phenotypic analysis- 5-FU



#### D Mitochondrial stress response to Paraquat from L4:



### CONCLUSIONS OF RESULTS 1:

- 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 is 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

Chemical	Maximum length	Growth dynamic	Fertility	Sexual maturity	Egg accum.	Embryog. survival	Larvae emergence	Larvae accum.	Repro toxicity	Conclusion	Toxic profil in vertebrate	Predictive
Phenitoïn	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Reprotoxicity	Toxic	Yes
Busulfan	333	333	333	333	333	333	333	333	333	Reprotoxicity	Toxic	Yes
Thiamazole	37	37	37	37	37	37	37	37	37	Reprotoxicity	Toxic	Yes
Dexamethasone	12	12	12	12	12	12	12	12	12	Reprotoxicity	Toxic	Yes
Progesterone	<1	<1	<1	<1	<1	<1	<1	<1	<1	No AE Observed	Negative	Yes
5-Fluorouracil	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Reprotoxicity	Toxic	Yes
Hydroxyurea	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Toxic	No
Methotrexate	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Embryotoxic effect	Toxic	Yes
Ascorbic acid	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Negative	Yes
Imatinib	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Reprotoxicity	Toxic	Yes
Diphenhydramine	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Negative	Yes
Lithium chloride	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Toxic	No
Methoxyacetic acid	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Toxic	No
Penicilin G	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Negative	Yes
Thalidomide	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Maternal AE	Toxic	Yes
Tetracycline	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Reprotoxicity	Toxic	Yes
Fingolimod	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Maternal AE	Toxic	Yes
Benzalkonium chl.	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Maternal AE	Toxic	Yes
Bisphenol A	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	Maternal AE	Toxic	Yes
Sodium Chloride	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Negative	Yes
Paraquat	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	No AE Observed	Toxic	No

### CONCLUSIONS OF RESULTS 2:

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;
3. Multi-phenotypic readouts in real-time.

5/5 negative chemicals confirmed

12/16 toxics/reprotoxics identified

17/20 with predicted outcomes

Balanced accuracy = 87.5%  
Sensitivity = 75%  
Specificity = 100%

**SydLab™ One represents the first «all-in-one» *C. elegans* lab-in-a-device that contributes to the rapid identification of toxic compounds in the early stages of drug discovery pipelines. Hence, making *C. elegans* now accessible for large safety and efficacy screenings as part of the NAMs toolkit.**