# *C. elegans* Automated Imaging Platform:

# De-risking drug candidates ahead of rodent studies with a non-mammalian model for ageing, neurodegeneration and the microbiome.

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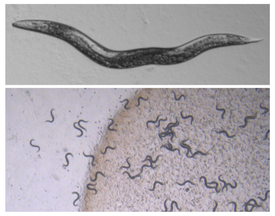
COVID-19 restrictions are slowing research productivity when drug development is needed most. Using the non-mammalian animal model *C. elegans*, Magnitude Biosciences is a UK-based CRO that can de-risk promising drug candidates before rodent testing.

## Why Worms?

**Relevant**
- ~ 40% genes have human orthologs
- Track record in ageing, neurodegeneration, cancer, metabolism
- Transgenics as models of inherited diseases
- Indicator species for pesticide toxicity with good concordance for known toxicity in mammals

**Efficient**
- Small : 1-2mm worms grown in Petri dishes
- Fast: development and 2-3 weeks lifespan
- Nematode: No regulatory restrictions
- Ethical: Reduces mammalian testing



Top: *C. elegans* worm, showing internal organs. Bottom: Worm population maintained on bacterial lawn in standard Petri dishes. Phase contrast microscopy.

**Versatile**
- Nervous system, muscle, intestine, epidermis and reproductive system
- Transparent body: easy live visualisation of eg. GFP-tagged targets
- Amenable to transgenics, from strain banks or customised in-house.
- Assays for developmental toxicity or life-long intervention effects

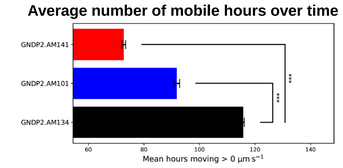
# Magnitude Biosciences

## *C. elegans* Research Services

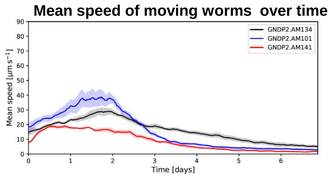
## Case Study: Neurodegeneration

*C. elegans'* amenability to genetic modifications makes it a versatile model for inherited diseases, especially those with mobility or age-related symptoms. Complex data analysis also allows for the detection of trade-off effects between duration and speed.

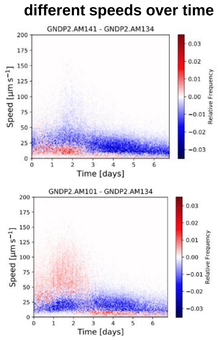
**Average number of mobile hours over time**



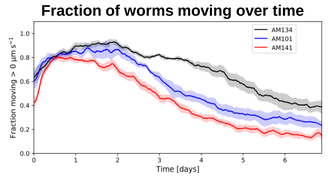

**Mean speed of moving worms over time**




**Gain or Loss of worms at different speeds over time**



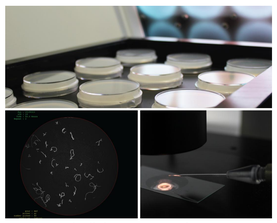

**Fraction of worms moving over time**




Multiple data analysis from a common dataset for **Huntington disease** model worms (PolyQ, 40 repeats): AM134 (control), AM 101(neuron expression), AM141 (muscle expression). Compared to controls, the muscle-expressing worms move the least often and are slowest throughout, while the neuron-expressing worms move less often but faster at early timepoints.

## Revolutionary Technology

- Up to 32 Petri dishes at a time automatically tracked by separate small cameras each controlled by a single board computer.
- Near-continuously movement tracking: images taken every 0.8 seconds for 160 seconds, repeated every 5 minutes, for up to 10 days of worm adulthood.
- Non-invasive: no mechanical disruption, no abrupt changes in lighting or temperature.
- Multiple mobility parameters : worm speed, position, percentage moving, population fragmentation by speed, speed decline over time, chemotaxis, exploration, paralysis, increases in population size in fertile worms.
- Standardised reagents, protocols and schedules for manual worm maintenance prior to automated assays
- Assays monitored remotely.

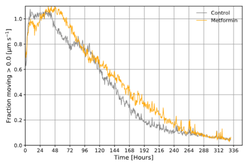


Top: Petri dish array set for illumination and image acquisition. Bottom Left: Representation worm tracks recording. Bottom Right: Micro-injection needle for transgenic strain generation.

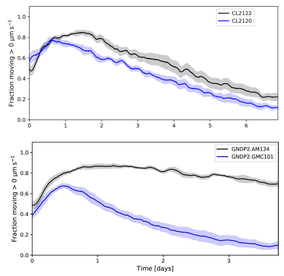
## Case Study: Ageing

*C. elegans'* short lifespan allows its use as a natural model of ageing, wherein mobility decline can be recorded to assess the effectiveness of anti-ageing candidates, or track the progression of age-related diseases.

**Metformin**
- Type 2 diabetes drug Involved in AMPK and mTORC1 regulation
- Improves lifespan in *C. elegans* and mice
- Improves cognitive function in humans (observed in diabetes trials)



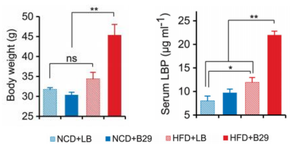

Percentage moving adult worms over 14 days imaging, showing a slower mobility decline over time in 50 mM metformin-treated worms.




**Alzheimer's disease** model strains in blue, showing more drastic mobility decline over time in the human-relevant muscle-expressing Aβ1-42 strain (GMC101, bottom) compared to muscle-expressing Aβ 3-42 strain (CL2120, top). black - Control strains

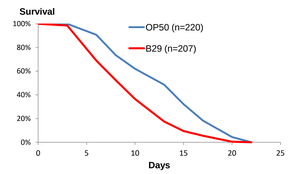
## Case Study: Microbiome

*C. elegans* is routinely maintained on a bacterial lawn, which makes it ideal for studying host-bacteria interactions, either by direct co-culture with compatible strains, or by addition of bacterial extracts .

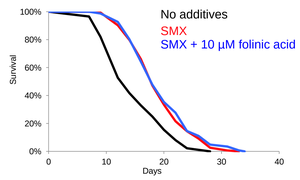



***Enterobacter cloacae* strain (B29), isolated from a morbidly obese human volunteer**, causes obesity in mice fed on a high-fate diet (HFD), but not in mice fed a normal chow diet (NCD). This correlates with an increase in serum LPS-binding protein (LBP), ,i.e. bacterial toxicity.

Data 16-weeks after inoculation.,- Advisor Board Member Liping Zhao Lab, (Fei & Zhao, 2013.).




*C. elegans* fed on B29 have a decreased lifespan compared to worms fed *on E. coli* (OP50). Data collected over 3 weeks. Data from Weinkove lab in collaboration with the Zhao lab.




**SMX** (sulfamethoxazole): Antibiotic disrupt excessive bacterial folate synthesis in OP50 *E. coli* and prevents likely mild toxicity by host-associated microbes (Virk *et al*., 2012 and 2016)

We believe that adoption of our C. elegans research services will boost drug pipeline productivity between *in vitro* and rodent studies, and strengthen the resilience of the biotech/pharma sector in these challenging times. For more info, www.magnitudebiosciences.com or email info@magnitudebiosciences.com