Unconventional genetics and ageing

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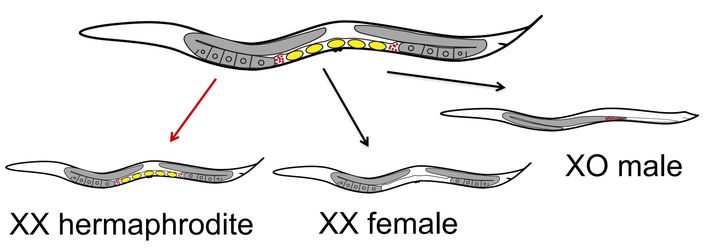
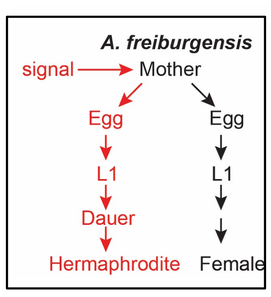
Introduction

We use nematodes (roundworms) as model systems to understand how experiences sensed by the mother are passed to the offspring (project 1), how and why programmed elimination of large pieces of DNA occurs (project 2) and uncover mechanisms that can delay the ageing process (project 3). We take advantage of the short lifecycle, short lifespan, and powerful genetic tools available to nematodes to study the mechanistic basis of these biological phenomena.

Project 1. Epigenetics: you are what your mother smelled

In *Auanema freiburgensis*, social cues (pheromones) are sensed by neurons. They transduce the environmental information to reprogram the germline, and thus the phenotype of next generation. After sensing the environment, the mother can determine the sex of the progeny in less than 24 hours.





Dauer induction in* A. freiburgensis *occurs across a generation. *If the mother senses pheromones, she produces stress-resistant larvae (dauer) that become hermaphrodites. Otherwise, she produces males and females.*

Goals:

- Downregulate maternal genes that influence epigenetic reprogramming
- Identify additional environmental cues influencing reprogramming of maternal germline

Reference:

Zuco et al (2018). Sensory neurons control heritable adaptation to stress through germline reprogramming. bioRxiv, 406033. https://doi.org/10.1101/406033

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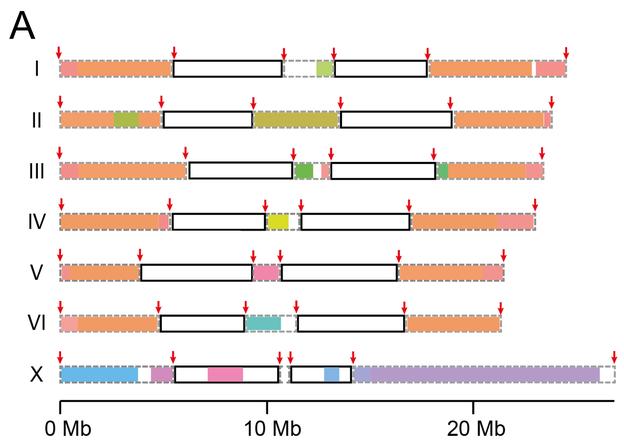
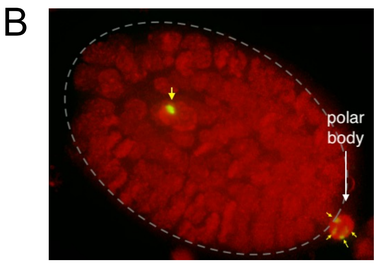
Project 2. Genetics: why and how do animals edit their own genomes?

In principle, all cells derived from a fertilised egg have the same genetic information. However, in some animals, specific genomic regions are removed from somatic cells during development. Why parts of the genome are removed from these cells, but not from cells forming the gametes (germline), has long remained an open question.





In the nematode *Auanema rhodensis*, 60% of the genome is discarded from the soma. *(A) Solid boxes represent sequences maintained in the soma for each chromosome, whereas stippled boxes represents portions that are discarded.Tandem repeats are colour-coded according to their sequences. Arrows represent target sites for the enzyme that mediates double-stranded breaks. (B) Embryo in which the germline-specific genome was labelled.*

Goals:

- Mutate germline-restricted genes
- Determine when during development DNA elimination occurs
- Prevent DNA removal in the somatic cells

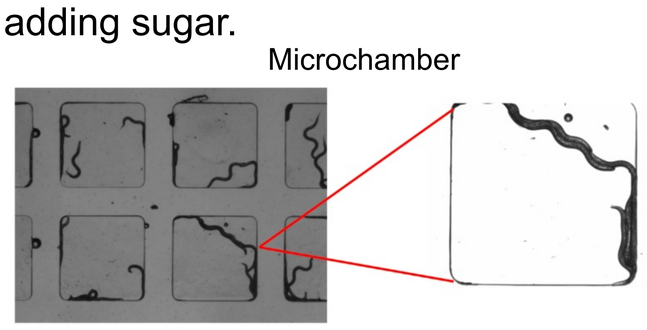
References:

Kloc, et al (2022). Natural genetic engineering: A programmed chromosome/DNA elimination. Developmental Biology *486*, 15-25.

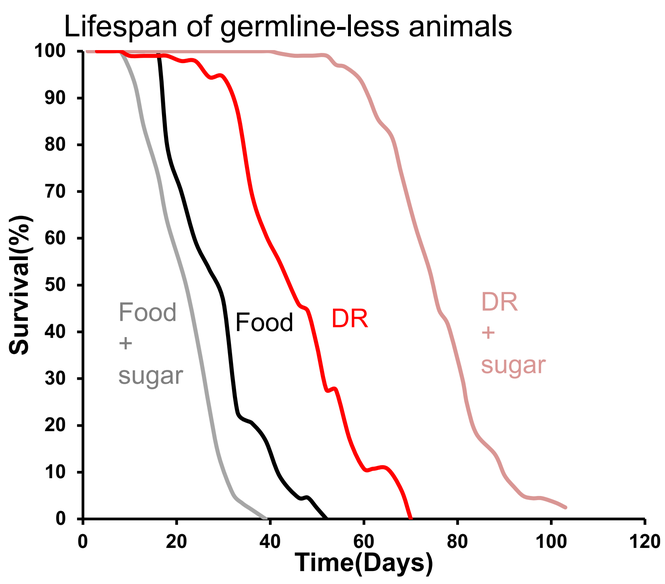
Wang et al (2014). Programmed DNA elimination in multicellular organisms. Curr Opin Genet Dev *27*, 26-34.

Project 3. Ageing: how to live 5x longer?

Certain manipulations, such as diet restriction (DR) and removal of the germline, can extend the lifespan of animals by 50% or longer. We found conditions that can make *C. elegans* to live even longer, by adding sugar.



Microchambers are used to trap nematodes and track them individually



Goals:

- Find genes responsible for extending lifespan under these conditions
- Determine if health span is also extendeds

Reference:

Hsin et al(1999). Signals from the reproductive system regulate the lifespan of *C. elegans*. Nature *399*, 362-366.