University of Leicester PhD studentship

Funding Source: CENTA DTP

Proposed start date: 23rd September 2024

Closing date for applications: See our web page

Eligibility: UK/International

Department/School: Genetics

Supervisors: **PI: Prof.** Eamonn Mallon (ebm3@le.ac.uk), University of Leicester

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Project Title: Early life environment changes how organisms age.

Project Description :

Project Highlights:

- Why individuals and species age so differently is an unanswered question in evolutionary biology.
- Diapause is an example of senescence plasticity, where the same genetics produces different ageing patterns in an organism.
- Using next-gen sequencing the project will measure DNA methylation across the genome of Nasonia and build the first insect epigenetic clock.

Overview:

This project will help understand why organisms age differently by establishing the effect of early life environments on epigenetic ageing in the model insect, *Nasonia vitripennis*. How individuals and species age so differently is one of the major unanswered questions in evolutionary biology with early life environments being a major predictor of lifespan.

Ageing is a mechanistically complex process influenced by many environmental and genetic components. The effects of these components influence each other, making them difficult to investigate, especially in complex mammalian models. Therefore, a large body of ageing research is based on simple model invertebrate organisms. Advantages include easy and inexpensive to keep in a laboratory, short life span, genetic and molecular tools available, and a sequenced genome.

However, current invertebrate ageing models (Drosophila and *C. elegans*) do not possess certain chemical marks (DNA methylation), an important part of how most organisms age. An epigenetic clock is a biochemical test based on measuring the accumulation of this DNA methylation. There is evidence that epigenetic clocks mirror true biological age and its associated morbidity and mortality better than chronological age in many species including us.

The jewel wasp, *Nasonia vitripennis*, an emerging model, has a functional methylation system, making it an ideal species to investigate the epigenetics of ageing. We have established an epige- netic clock in this species.

Early life effects on ageing have pervasive influence on the ecology and evolution of a range of species from fish to birds to humans. It would be useful to study a dramatic example, where a distinct early

life environment lead to a dramatic switch in ageing strategy, a so-called senescence plasticity. An example of this is larval diapause in *Nasonia* where if the mother experiences autumn-like conditions, her larval offspring become dorminant over winter and then as adults live much longer than adult Nasonia who haven't overwintered.

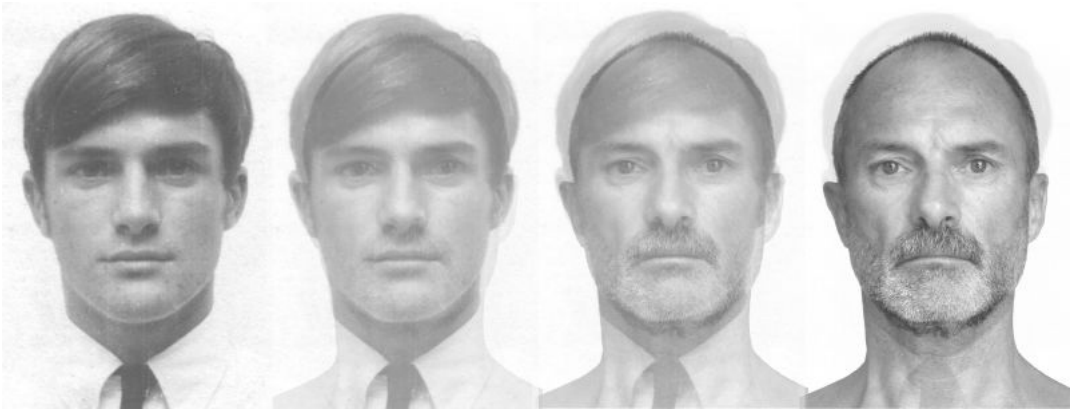

Figure 1: Early life environments seem to be one of the most important factors in how an organism ages.

Alt text Photos of the same man ageing from young adulthood to late middle age.

Methodology:

This project combines whole genome bisulfite sequencing of Nasonia, machine learning, RNAi knockdowns of methylation enzymes and high-throughput behavioural analysis, to analyse chronological and epigenetic ageing in diapaused and non-diapaused Nasonia.

References:

- Horvath, S. DNA methylation age of human tissues and cell types. *Genome Biol* **14**, 3156 (2013). https://doi.org/10.1186/gb-2013-14-10-r115. The original paper that discovered epigenetic clocks in humans.
- Pinho, G.M., Martin, J.G.A., Farrell, C. *et al.* Hibernation slows epigenetic ageing in yellow-bellied marmots. *Nat Ecol Evol* **6**, 418–426 (2022). https://doi.org/10.1038/s41559-022-01679-1. A paper showing a very clear effect of mammalian hibernation on epigenetic ageing.
- Brink K., Thomas C., Jones A. , Mallon E.B. An epigenetic clock in an insect model system bioRxiv 2023.02.14.528436. https://doi.org/10.1101/2023.02.14.528436. Our preprint with the discovery of an insect epigenetic clock.

Funding details:

NERC CENTA studentships are for 3.5 years and are funded by NERC. In addition to the full payment of your tuition fees, you will receive the following financial support:

- Annual stipend, currently set at £18,622 (2023/4 – new figures to be confirmed spring 2024)
- Research training support grant £8,000 (RTSG)

If you are not eligible for UK Fees the University of Leicester will fund the difference between UK and International fees for the duration of your studies

For more details of the CENTA consortium please see the CENTA website: www.centa.org.uk.

Entry requirements:
Applicants are required to hold/or expect to obtain a UK Bachelor Degree 2:1 or better in a relevant subject.

The University of Leicester English language requirements apply where applicable.

Application advice:

To apply please refer to our web page for further information and read carefully the How to Apply section before submitting your application
https://le.ac.uk/study/research-degrees/funded-opportunities/centa-phd-studentships

In the funding section please specify that you wish to be considered for Ref CENTA2-GENE1-MALL

In the proposal section please provide the name of the supervisors and project title (a proposal is not required)

Project / Funding Enquiries to: CENTA@le.ac.uk or ebm3@le.ac.uk

Application enquiries to pgradmissions@le.ac.uk