**University of Leicester**

**BBSRC MIBTP Studentship Project 2025-6 entry.**

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**Section 2 – *Project Information***

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| **Project Title** | The Epigenetic Basis of Longevity: Calorie Restriction and Ageing in *Nasonia vitripennis*  |
| **Project Summary**  |
| his project will establish *Nasonia vitripennis*, a parasitic wasp, as a model organism to study the mechanisms of ageing, with a specific focus on the relationship between calorie restriction and epigenetic ageing. We are particularly interested in how changes in DNA methylation—the addition of chemical marks to DNA molecules—impact biological age and lifespan. **Background** Ageing is a complex process, influenced by environmental and genetic factors. Traditionally, chronological age (the number of years an organism has lived) has been used to measure ageing. However, recent research indicates that *epigenetic age*, which is based on the accumulation of DNA modifications like methylation, may more accurately reflect an individual’s biological age, predicting health and longevity more effectively. Epigenetic clocks, which use DNA methylation to estimate biological age, have been discovered in various organisms. However, understanding the underlying mechanisms remains challenging. This project aims to explore how epigenetic clocks work and how they might be influenced by lifestyle factors such as calorie intake. **Why *Nasonia vitripennis*?** While existing invertebrate models of ageing, such as *Drosophila melanogaster* (fruit flies) and *Caenorhabditis elegans* (nematodes), have provided valuable insights into the ageing process, they do not have a detectable DNA methylation system, limiting their utility for epigenetic studies. *Nasonia vitripennis*, on the other hand, has a functional DNA methylation system, making it an ideal candidate for studying the epigenetics of ageing. We have discovered an epigenetic clock in *Nasonia*, marking the first time such a clock has been identified in a tractable insect model. This breakthrough allows us to measure the epigenetic age of individual wasps and track how it changes over time in response to environmental factors like calorie intake. **The Role of Calorie Restriction** Calorie restriction, the practice of reducing calorie intake without causing malnutrition, has been one of the most effective ways to increase lifespan across a wide variety of organisms, from yeast to mammals. In *Nasonia*, reducing the sugar content of their diet from 30% to 10% has been shown to increase lifespan by approximately 20%. This project will investigate how calorie restriction affects both the lifespan and epigenetic ageing of *Nasonia*. Specifically, we hypothesize that: 1. **Calorie restriction will slow the rate of epigenetic ageing** in *Nasonia*.
2. **The beneficial effects of calorie restriction on lifespan and healthspan** (as measured by behavioral assessments) will be disrupted by treatments that reduce DNA methylation, suggesting that the epigenetic clock plays a key role in mediating these effects.

**Methods** We will use oxford nanopore sequencing to measure DNA methylation and determine the epigenetic age of *Nasonia*. In addition, behavioural assays will be conducted to assess healthspan (the period of life spent in good health), while lifespan will be recorded under different caloric restriction conditions. By comparing these results with those of *Nasonia* subjected to DNA methylation-reducing treatments, we hope to establish a direct link between calorie restriction, epigenetic ageing, and longevity. **Objectives** This project has several key objectives: * To further establish *Nasonia vitripennis* as a powerful model for studying epigenetic ageing.
* To explore the effects of calorie restriction on both chronological and epigenetic ageing.
* To investigate the role of DNA methylation in mediating the lifespan and healthspan-enhancing effects of calorie restriction.

**Impact and Opportunities** As a PhD candidate, you will gain experience in cutting-edge molecular biology techniques, such as oxford nanopre sequencing, alongside behavioral studies and lifespan analyses. The project will contribute to the growing field of epigenetic ageing, with potential applications ranging from age-related disease prevention to interventions that promote healthy ageing. Techniques that will be undertaken during the projectThis project combines oxford nanopore sequencing of *Nasonia*, machine learning, RNAi knockdowns of methylation enzymes and high-throughput behavioural analysis, to analyse chronological and epigenetic ageing in calorie-restricted and control *Nasonia*.  |
| **References** |
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