Project title: Genetic and environmental variation in the effect of dietary restriction on life-history trade-offs and ageing in *Drosophila*.

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Background: Understanding the causes and consequences of variation in longevity and ageing is important not only in the context of life history evolution, but also in our attempts to understand and mitigate these processes in humans. Life history theory predicts that variation in longevity and ageing is related to the trade-off between survival and reproduction. Dietary restriction (DR), a modest reduction in nutrient intake, has been shown to increase longevity and slow rates of ageing across a diverse range of species. The evolutionary explanation for this prolongevity effect of DR is that it alters the trade-off between survival and reproduction in the favour of increased investment in survival. Although the effect of DR is thought to be evolutionarily conserved, recent studies suggest genetic variation in the response to DR. In addition, recent theory has questioned whether the prolongevity and anti-ageing effect of DR will persist when organisms are exposed to ecologically relevant stressors such as pathogens, physical injury and temperature variation. Understanding the extent of this variation in the response of longevity and ageing to diet is clearly important in improving our understanding of the ageing process, how it might be mediated by diet and how this may vary between individuals and environments. This project will use *Drosophila melanogaster* as a model organism in which to provide detailed studies of genetic variation in the response to DR and the effect of exposure to environmental stress.

Drosophila melanogaster in the wild. ©Darren Obbard

Key research questions: How much genetic variation is there in the response to dietary restriction? How does dietary restriction alter the genetic correlations between life history traits? Does exposure to environmental stress remove the longevity benefit of dietary restriction?

Methodology: These questions will be investigated by rearing *Drosophila melanogaster* on diets that vary in macronutrient composition and assaying life history traits such as survival and reproduction under different environments. Experiments in the first two years will involve using the Drosophila Genetic Reference Panel (DGRP) (~ 200 inbred lines of Drosophila) to perform quantitative genetic experiments to allow estimation of the quantitative genetic variation in the response to DR and how DR influences the genetic (co)variation between life history traits. The existence of genome wide sequence data for these lines will allow investigation of candidate genes underlying this variation. In the third year, Drosophila reared different diets will be exposed to environmental stressors including pathogens, physical injury and temperature variation to assess the effect of environmental variation on the response to DR.

Training: A comprehensive training programme will be provided comprising both specialist scientific training and generic transferable and professional skills. More specifically students

will receive training in the design, implementation and analysis of complex multi-generational experiments including quantitative genetic experiments. Students will also receive training in the care and maintenance of experimental animals and in the measurement of numerous behavioural, physiological and life history traits.

Requirements: Candidates should possess at least a 2-1 hons degree or its equivalent in a biology related subject and a strong interest in evolutionary ecology, ageing or related disciplines. Ideally candidates would be able to demonstrate experience in research in a relevant field and show strong evidence of independent thinking. This project will involve large scale experiments that will require good time management and planning skills. Training in statistical analysis will be provided but previous experience with large scale life history or behavioural experiments and their analysis would be a benefit.

References:

Adler, M. I., and R. Bonduriansky, 2014 Why do the well-fed appear to die young? BioEssays **36:** 439-450.

Liao, C.-Y., B. A. Rikke, T. E. Johnson, V. Diaz and J. F. Nelson, 2010 Genetic variation in the murine lifespan response to dietary restriction: From life extension to life shortening. Aging Cell **9:** 92-95.

Nakagawa, S., M. Lagisz, K. L. Hector and H. G. Spencer, 2012 Comparative and meta-analytic insights into life extension via dietary restriction. Aging Cell **11:** 401-409.

Project summary (30 words): This project will investigate genetic variation in the response to dietary restriction and whether exposure to environmental stress removes the longevity benefit of dietary restriction.