Summer Studentships 2022 Projects List

Host Unit: Alic lab, Institute of Healthy Ageing

Supervisor: Dr Nazif Alic

Project Title: The ability of long-lived mutants to maintain metabolic homeostasis in old age

Project outline

Alterations to metabolic homeostasis, which can result in obesity and insulin-resistance (type II diabetes) are an ever-growing concern to our society, and are at least in part due to the caloric excess of our modern diet. Both obesity and insulin-resistance have a complex interaction with a person's age. Recent exciting work in biogerontology has discovered interventions that can extend lifespan in organisms as diverse as the fruit fly and mammals. However, it remains unclear whether longevity extending manipulations can lead to better metabolic homeostasis and counteract poor diet choices, preventing obesity and insulin-resistance. This project will examine if mutations that can make the fruit fly live longer can also rescue from the effects of poor diet, using a range of techniques in fly physiology and molecular and cell biology.

***Deadline for contact*:**

10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: n.alic@ucl.ac.uk

Host Unit: Jon Bridle Group, Centre for Life's Origins and Evolution

Supervisor: Jon Bridle

Project Title: Testing limits to adaptive plasticity in Sicilian daisies

A key question given rapid climate change is the degree to which existing phenotypic plasticity will allow populations and species to behave appropriately in novel environmental regimes. Theory suggests that existing plasticity should buffer fitness loss within existing environmental variation, but is likely to fail as past environmental conditions are exceeded. We are testing these hypotheses using: (1) field assays of phenotype, gene expression and fitness in Senecio daisies along elevational gradients on Mount Etna, Sicily; (2) Experimental crossing and rearing of genotypes in greenhouses at UCL and in Sicily. This project would use either or both of these approaches, in collaboration with the University of Catania. This project would be ideal for students passionate about population genetics and evolution, wanting experience in field transplant techniques and/or quantitative genetics and phenotypic assays (or both).

***Deadline for contact*:**

10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: j.bridle@ucl.ac.uk

Host Unit: Florencia Camus Group, Centre for Life's Origins and Evolution
Supervisor: Dr. Florencia Camus
Project Title: Understanding the role of metabolic genes in adaptation

Metabolism lies at the core of organismal survival and reproduction. Mitochondria are key to metabolic adaptation as they provide the hub that converts food into energy. This process is complicated by the fact that mitochondrial function relies on genes from two different genomes – nuclear and mitochondrial. Their harmonious interaction is essential for organismal viability. We expect rapid coevolution between mitochondrial and nuclear encoded respiratory genes to occur within populations. Coevolution should also consider the environment these populations are adapting to, with rapid environmental change predicted to have massive impact on metabolism. Indeed, evidence suggests that intergenomic matching could impact the phenotypic responses to dietary and temperature variations.

This project will aim to examine how mito-nuclear genotypes impact thermal tolerance traits in Drosophila melanogaster. We have source flies from the east coast of Australia, where we know that the north and south populations differ in thermal tolerance traits. Interestingly, there are also large genetic differences with populations from the north and south of Australia having different mtDNA genomes. Using genetic tools specific to Drosophila, we can manipulate genomes, and have created several new strains of fly that have either matched (north-north, south-south) or mismatched (north-south, south-north) mito-nuclear genomes. Using these genetic tools we will be able to fully understand the contribution of both these genomes, plus their interaction, to the process of thermal adaptation.

***Deadline for contact*:**
10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: f.camus@ucl.ac.uk

Host Unit: Genome Regulation Lab (PI: J. Bähler), Institute of Healthy Ageing
Supervisor: Dr Ben Heineike
Project Title: Genetic basis of biofilms in fission yeast

Project outline

Quantitative Trait Locus (QTL) analysis is a powerful tool that links genotypes to phenotypes. To perform this technique, two closely related strains of an organism which differ in some phenotype of interest are mated and the phenotype is measured in a set of sequenced hybrid progeny. One can then attempt to identify the genomic basis for the phenotype. Our lab has developed a protocol for applying QTL analysis in the important model organism, *Schizosaccharomyces pombe* (fission yeast), and have a set of sequenced hybrid progeny from two parental strains which vary with respect to a number of traits. We have recently observed that the two parental strains show a striking variation in terms of their tendency to stick to glass flasks when cultured.

In this project the student will record this biofilm-forming phenotype in the hybrid progeny and conduct QTL analysis to identify the genetic differences responsible for this phenotype.

No specific knowledge is required in order to perform the experimental portion of this projects. For the QTL analysis, an interest in genetics and some background in statistics and computational data analysis would be helpful

***Deadline for contact*:**
10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: benjamin.heineike@crick.ac.uk

Host unit: Gems lab, Institute of Healthy Ageing

Supervisor: Prof. David Gems

Project Title: Biology of Ageing in *C. elegans*

Project outline

The project will involve some aspect of the biology of ageing in *C. elegans*, to be determined closer to the date of the project.

While developmental genetics has been an area of intensive study for many years, investigation of the role of genes in determining longevity and ageing only recently began. An ideal model organism in which to study ageing is the free-living nematode *Caenorhabditis elegans*. This species has well-developed genetics, its 97,000,000 base pair genome is fully sequenced, and its life span is a mere 2-3 weeks. Most importantly, numerous mutations have been identified in *C. elegans* which alter the rate of ageing, with some mutants living more than five times as long as wild-type worms. It is hoped that by understanding ageing in a simple animal like *C. elegans* we will be able to unravel the mystery of human ageing, which increases risk of a wide range of diseases, from cardiovascular disease and type II diabetes, to Alzheimer's disease and cancer.

A major focus of current work in this laboratory is understanding the genes and biochemical processes by which reduced insulin/IGF-1 signalling and dietary restriction increase lifespan. Other interests include sex differences in the biology of ageing, evolutionary conservation of mechanisms of ageing, and bioethical implications of ageing research.

Special requirements

These projects are suited for students who are considering a possible future career in scientific research. A good grounding in genetics is helpful.

Deadline for contact

10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: david.gems@ucl.ac.uk

Host unit: Nick Lane's research group, Centre for Life's Origins and Evolution
Supervisor: Prof. Nick Lane

Project 1 title: How energy flow structures metabolism and heredity at the origin of life.

Project 1 description

How energy flow structures metabolism and heredity at the origin of life.
We have several experimental and computational projects that address different aspects of the origin of life from an energetic perspective, specifically how the first cells came to be powered by proton gradients across membranes. The student would be able to choose, depending on their interests and progress in the meantime, between projects on CO2 reduction across inorganic barriers, the behaviour of fatty acid protocells, aspects of nucleotide synthesis, and interactions between amino acids and nucleotides. Computational projects would focus on the origin of the genetic code in relation to the coevolution of metabolism and the code.

Project 2 title: How mitonuclear interactions shape mitochondrial function and fitness in *Drosophila*

Project 2 description

This work would be in collaboration with Dr Flo Camus and uses a well-established fruit fly model to study mitonuclear incompatibilities. Several different projects would be available depending on the interest of the student and progress in the meantime, ranging from fluorespirometry using the Oroboros O2K to measure mitochondrial function, to analysis of metabolomic and proteomic datasets, to exploration of phenotypes in flies, ranging from male or female fitness to activity and lifespan. Projects could relate to the effects of diet, temperature and drug responses with a focus on overall physiology or brain-specific metabolism linked to dementia.

Deadline for contact

10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: nick.lane@ucl.ac.uk

Host unit: Andrew Pomiankowski's research group, Centre for Life's Origins and Evolution
Primary Supervisor: Prof Andrew Pomiankowski
Secondary Supervisor: Prof Nick Lane

Project 1 Title: The metabolic costs of an exaggerated sexual ornament in stalk-eyed flies

Male stalk-eyed flies have highly exaggerated eyespan. This is a classic example of sexual selection, caused by strong female mate preferences for males with wider eyespan. We know this trait imposes aerodynamic costs on males (they take-off at a lower angle, due to the extra head weight), it slows development (males take 1-2 extra days to emerge from pupae) and is a highly condition-dependent trait (being very sensitive to environmental and genetic stress). Eyespan is a means for females to assess male phenotypic and genetic quality. The project will break new ground in examining the energetic costs of exaggeration. The student will measure a range of metabolic parameters in males, e.g. oxygen consumption and reactive oxygen species (ROS) flux. By introducing different substrates, the performance of mitochondrial complexes I-IV can be assessed under environmental stress. These features of the energetic state will be compared across males with different eyespan exaggeration. The student will compare different tissues (head, thorax and reproductive organs) in males and females, as well in larvae when eyespan size is determined. We hypothesize that metabolic trade-offs between investment in growth and development versus aerobic capacity for flight and aerodynamics underpin differences in eyespan, with the honesty of the handicap signal primarily reflecting metabolic fitness.

References

Finnegan, S.R., White, N.J., Koh, D., Camus, M.F., Fowler, K. and Pomiankowski, A. 2019 Meiotic drive reduces egg-to-adult viability in stalk-eyed flies. **Proceedings of the Royal Society London B** 286, 20191414

Meade, L., Finnegan, S.R., Kad, R., Fowler, K. and Pomiankowski, A. 2020 Maintenance of fertility in the face of meiotic drive. **American Naturalist** 195(4), 743-751.

Howie, J., Pomiankowski, A. and Fowler, K. 2019 Limits to environmental masking quality in sexual signals. **Journal of Evolutionary Biology** 32, 868-877.

Project 2 Title: How does a selfish genetic element affect female sexual activity?
Primary Supervisor: Prof. Andrew Pomiankowski
Secondary Supervisor: Prof. Jon Bridle

Meiotic drivers are selfish genetic elements that disrupt normal gamete production during meiosis (Lindholm *et al.* 2016). We are interested in an X-linked meiotic drive system, *Sex Ratio* (SR), in the stalk-eyed fly, *Teleopsis dalmanni*. In males, drive causes Y-bearing sperm to degenerate, only the SR chromosome is transmitted, resulting in all-female broods. The two-fold advantage in transmission gained by drive is offset by a range of disadvantages to SR males. Male egg-to-adult survival is reduced when they carry the drive chromosome, they have reduced eyespan – a trait used by females in mate choice – and their fertility is impaired under sperm competition (Cotton *et al.* 2013; Finnegan *et al.* 2019, 2021; Meade et al. 2020). But what are the fitness impacts of drive in females? We already know that drive reduces female egg-to-adult survival, with a higher survival cost in homozygous females (Finnegan *et al.* 2019). The student will investigate several important components of reproductive fitness: (1) the time to sexual maturity (stalk-eyed flies take several weeks to mature), (2) female fecundity and (3) female mate preference. These will be studied in female heterozygotes and homozygotes. This will give a much better understanding of constraints on the spread of meiotic drive.

References

Cotton, A. J., Földvári, M. Cotton, S. and Pomiankowski, A. 2014 **Heredity** 112, 363-369.

Finnegan, S.R., White, N.J., Koh, D., Camus, M.F., Fowler, K. and Pomiankowski, A. 2019 **Proceedings of the Royal Society London B** 286, 20191414.

Finnegan, S.R. 2021 **Journal of Evolutionary Biology** 34, 736-745.

Lindholm, A. K. 2016 **Trends in Ecology and Evolution** 31, 315-326.

Meade, L., Finnegan, S.R., Kad, R., Fowler, K. and Pomiankowski, A. 2020 **American Naturalist** 195(4), 743-751.

Deadline for contact

10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: Prof. Andrew Pomiankowski (ucbhpom@ucl.ac.uk)

Host Unit: Shou lab, Centre for Life's Origins and Evolution

Supervisor: Prof Wenying Shou

Project Title: Understanding the dynamics of autophagy using the GFP-Atg8 assay and mathematical modelling

Project outline

When cells encounter stresses such as nutrient starvation, they can trigger autophagy where intracellular components are degraded to support processes essential for survival. Autophagy starts as a double-membraned structure called the phagophore, which grows to envelope the targets of degradation. Autophagy is generally monitored using the GFP-Atg8 cleavage assay where one quantifies the ratio of GFP-Atg8 (prior to autophagic degradation) to GFP (a relatively stable product after autophagic degradation). The GFP-Atg8 assay is frequently performed only at a single timepoint, and it is unclear how representative this "snapshot" is of the possible dynamics of autophagy. Here, we will use the budding yeast S. cerevisiae to experimentally test a prediction of our mathematical model. Our model predicts that in the absence of desensitisation, autophagy activity will reach a steady state. We will starve wild type yeast cells of various types of nutrients (e.g. nitrogen and sulphur), and measure autophagy activity over time. In the future, we will test other predictions of the model (e.g. which aspects of the autophagy pathway are or are not captured by the GFP-Atg8 assay). This will help researchers to better understand the dynamics of autophagy as well as the meaning of the assay.

***Deadline for contact*:**

10 January 2022. Applicants should send a cover letter, brief CV & contact details of a referee.

Contact: w.shou@ucl.ac.uk