The University of Sheffield

Faculty of Medicine, Dentistry & Health

(Department/School name)

**Project title: Investigating the control and function of macrophage subtypes using *Drosophila melanogaster***

**Supervisor(s):** Iwan Evans

**Project details:**

The phagocytic white blood cells known as macrophages are a highly heterogeneous population of cells. This heterogeneity stems from their differentiation from monocytes, the presence of tissue resident cells and their ability to polarise to a wide range of activation states. This diversity enables macrophages to carry out their complex and varied physiological roles, which range from host defence to homeostasis, regeneration and repair.

We use the fruit fly (*Drosophila melanogaster*) to understand regulation of the innate immune system, taking advantage of this organism’s lack of genetic redundancy, excellent genetic tools and imaging capabilities and the presence of blood cells called hemocytes. Hemocytes are comprised of three types of cell, one of which is a macrophage lineage also known as plasmatocytes (Ratheesh et al., 2015). These macrophages are critical for normal development and immunity of this organism (Defaye et al., 2009). Until recently *Drosophila* macrophages were considered to be a uniform population of cells. However, for the first time, we have identified subpopulations of functionally-distinct *Drosophila* macrophages (Coates et al., 2020).

The aims of this project are to understand how these macrophage subpopulations are specified and their roles across the lifecourse. These subpopulations are highly plastic and developmentally-regulated and exhibit specific localisations in the adult, suggesting they may represent tissue resident macrophage populations in the fly. This work will uncover how innate immune diversity can be generated and controlled in the absence of adaptive immunity and will therefore shed light on the evolution of the immune system alongside identifying novel mechanisms controlling immune cell function and localisation.

This project involves fly genetics, molecular biology, cell biology techniques, live cell imaging, confocal microscopy and image analysis. The project will be hosted in the world-leading Bateson Centre at the University of Sheffield, which aims to use non-mammalian model organisms to understand developmental biology and human disease processes.

**References:**

Ratheesh, A., Belyaeva, V. & Siekhaus, D. E. Drosophila immune cell migration and adhesion during embryonic development and larval immune responses. Current Opinion in Cell Biology 36, 71–79 (2015).

Defaye, A. et al. Genetic ablation of Drosophila phagocytes reveals their contribution to both development and resistance to bacterial infection. J. Innate Immun. 1, 322–334 (2009).

Coates, J. A., Brittle, A., Armitage, E. L., Zeidler, M. P. & Evans, I. R. Identification of functionally-distinct macrophage subpopulations regulated by efferocytosis in Drosophila. bioRxiv 2020.04.17.047472 (2020). doi:10.1101/2020.04.17.047472

**Funding:**

This project is suitable for a self-funded student or a student with a government scholarship including from overseas.

**Entry Requirements:**

Candidates must have a first or upper second class honors degree or significant research experience.

**Enquiries:**

Interested candidates should in the first instance contact Iwan Evans (i.r.evans@sheffield.ac.uk). Please visit <http://iwanrevans.weebly.com/> for more information about the Evans lab.

**How to apply:**

Please complete a University Postgraduate Research Application form available here: [www.shef.ac.uk/postgraduate/research/apply](http://www.shef.ac.uk/postgraduate/research/apply)

Please clearly state the prospective main supervisor in the respective box and select Department of Infection, Immunity and Cardiovascular Disease as the department.

**Closing date: *(please enter closing date for applications here)***

Proposed start date: applications are accepted all year round

Salary/stipend rate:

Please advise on categories for advertisement on findaphd.com (tick up to ten):

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