The University of Sheffield

Faculty of Medicine, Dentistry & Health

(Department/School name)

**Project title: Identifying novel regulators of haematopoiesis using flies**

**Supervisor(s):** Iwan Evans (primary supervisor); Steve Brown (BMS, secondary supervisor)

**Project details:**

Control of blood cell proliferation, survival and activation is critical to the health of an organism. Defects in this control can lead to a wide range of diseases or pathological conditions including cancer, immunodeficiencies or autoimmunity. Knockout studies in higher organisms can lead to embryonic lethality precluding their study without the time-consuming and expensive generation of additional genetic tools. The use of simpler organisms such as the fruit fly, *Drosophila melanogaster*, in which numerous genome-wide reagents are already available, additionally avoids the ethical constraints that need to be considered when working with protected organisms such as mice. Furthermore, flies represent a cheaper and more high-throughput approach, with key pathways conserved between this organism and higher vertebrates (Banerjee et al., 2019).

*Drosophila* has been widely usedto dissect genetic regulation of blood cell specification and proliferation, taking advantage of this organism’s lack of genetic redundancy, excellent genetic tools and imaging capabilities and the presence of blood cells called hemocytes. (Ratheesh et al., 2015). These blood cells are critical for normal development and immunity of this organism (Defaye et al., 2009). We have undertaken a genome-wide association study and uncovered numerous novel regulators of haematopoiesis and cell activation in *Drosophila*. This project will examine the validated hits from this genetic screen in order to understand their mechanism(s) of action. The successful candidate will use high-throughput screening approaches within the University of Sheffield’s RNAi Screening Facility alongside live imaging and cell biological analyses of blood cells in vivo. Candidate genes will be investigated using fly genetics to identify the pathways these genes act through and the tissues in which gene activity is required.

This project therefore involves fly genetics, cell culture, molecular biology, cell biology techniques, live cell imaging, confocal and hi-content 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:**

1. Banerjee, U., Girard, J. R., Goins, L. M. & Spratford, C. M. Drosophila as a Genetic Model for Hematopoiesis. Genetics 211, 367–417 (2019).

2. 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).

3. 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).

**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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