

Department of Veterinary Medicine

Available PhD Project:

Supervisors: Dr Raymond Bujdoso

Supervisor profile pages:

<https://www.research.vet.cam.ac.uk/research-staff-directory/principal-investigators/infection-and-immunity/Raymond-Bujdoso>

Project Title: Identification of genetic modifiers of prion-induced neurodegeneration

Background: Prion diseases are fatal transmissible neurodegenerative diseases of various mammalian species. The emergence of atypical BSE in cattle and new reservoirs of CWD in cervids pose fresh challenges to human food safety since their zoonotic potential is unknown. Central to prion diseases is the conversion of the normal host protein PrP^C into the abnormal conformer PrP^{Sc}. The 'protein only' hypothesis proposes that the infectious agent responsible for the transmission of prion disease comprises principally PrP^{Sc}, which is also considered to be responsible for neurotoxicity. It is important to characterise genetic modifiers of cellular events that participate in prion-induced neurodegeneration as this knowledge will underpin the development of new diagnostic markers for prion disease, breeding programmes for the generation of prion disease-resistant animals for the purpose of food safety and therapeutic targets for these currently untreatable diseases.

We have established *Drosophila* models of acquired and genetic forms of mammalian prion disease to probe the mechanism of prion-induced neurotoxicity in a tractable genetically well-defined host. Our novel studies have shown that prion-infected PrP transgenic *Drosophila* demonstrate hallmark features of mammalian prion disease and provide the basis to study fundamental features of bona fide prion-propagation in a new versatile animal host.

This PhD project will identify genetic modifiers of prion-induced neurodegeneration by the following approach. RNA-Seq-based whole transcriptome and mass spec-based proteomic analysis will be performed on the brains of prion-infected PrP transgenic *Drosophila*. Bio-informatic analysis will be performed on the resultant gene expression data sets to identify the biochemical and cellular events affected by prion infection. Candidate genes from the different biochemical pathways affected by prion infection in PrP transgenic *Drosophila* will be screened for their effect on prion replication and prion-induced neurotoxicity by RNAi-mediated knockdown. This is a novel inter-disciplinary project at the cutting edge of protein misfolding-induced neurodegeneration research.

More info here: <http://www.cam.ac.uk/research/news/fruit-fly-model-of-deadly-brain-diseases-could-lead-to-blood-test-for-vcjd>

BBSRC DTP: As a Targeted BBSRC DTP student the successful candidate will complete DTP training courses and will undertake two rotation projects in their first year (one in their PhD laboratory and a second in a lab of their/their Supervisor's choosing. On successful completion of these, they proceed to their PhD project. Students must also complete a three-month internship (PIPS), usually before the last six months of the Programme. The full programme must be completed within 48 months.

Funding:

Full scholarship for UK residents: UK and EEA students who meet the UK residency requirements ([see here](#)) will be eligible for a full 4 year BBSRC studentship. This will cover a stipend at the standard Research Council rate (£14,553 per annum for 2017/18), research costs and tuition fees at the UK/EU rate, to start 1st October 2018.

How to apply:

- Preliminary Stage: Please send your CV, transcripts and a cover letter to Fiona Roby (email: fr288@cam.ac.uk) **by 31st January 2018**. The cover letter should outline your research interests and experience and explain why you think you would be a good fit for this project. Please also include contact details for two referees who may be contacted in the event you are shortlisted. Shortlisted candidates will be invited to interview in February 2018 (date subject to change).
- Secondary Stage (only if successful at interview stage): Following interviews the successful candidate will then need to submit a full official application to the University of Cambridge via the [Applicant Portal](#) - note there is a £50 fee for this application. A full offer will only be made once all conditions required by the University have been met.

Deadline to apply: 31st January 2018