

Department of Veterinary Medicine: PhD Project

Project Title: The mechanisms by which disease-inducing mutations trigger innate immune signalling proteins

Supervisor: Professor Clare Bryant

Supervisor profile page: <https://www.vet.cam.ac.uk/directory/ceb27%40cam.ac.uk>

Project details: Innate immunity is the first line of defence against infection. It is now clear there are many mutations in innate immunity genes from Toll-like receptor (TLRs) and inflammasome signalling pathways that trigger hyper-inflammatory syndromes and severe autoimmunity. TLRs and inflammasomes signal via the formation of large signalling complexes. We have identified the how these signalling complexes form in cells and identified the physiological consequences when one or more proteins are removed¹⁻³. A number of diseases are caused by genetic mutations in TLR or inflammasome signalling proteins, but how these cause disruption or autoactivation of signalling is unclear. In this project we will use CRISPR/Cas9 to introduce disease inducing mutations into innate immune genes and characterise their effects on infection control, cell death, cytokine production and the formation of macromolecular signalling platforms using a range of cell biology, biophysical and imaging techniques.

The skills to be learnt by the student in this project will be:

- Basic comparative bioinformatic analysis of genes in the innate immune system
- Cell culture and cellular infection techniques
- CRISPR/Cas9 gene editing of human cell lines to modify innate immune genes
- Analytical techniques including imaging, FACs, ELISA, PCR and western blot analysis.
- Writing, presentation and literature analysis techniques

References:

1 doi.org/10.1101/2021.09.20.461078

2 doi: 10.1073/pnas.1402911111

3 doi: 10.1038/s41564-020-00801-y

Funding: This project is open to self-funding students or students wishing to apply for the Cambridge Postgraduate Funding competition. More info here:

<https://www.postgraduate.study.cam.ac.uk/funding-overview/university-funding>

How to apply: Contact the Supervisor (ceb27@cam.ac.uk) to discuss the project before submitting an official application. More here on application process here:

[PhD in Biological Sciences at the Department of Veterinary Medicine | Postgraduate Admissions \(cam.ac.uk\)](https://www.vet.cam.ac.uk/postgraduate-admissions)