

Department of Veterinary Medicine: PhD Project

Project Title: How do evolutionary changes in innate immune genes influence host susceptibility to infection with zoonotic pathogens

Supervisor: Professor Clare Bryant

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

Project details: Zoonotic pathogens, such as COVID-19, reside in animal hosts before jumping species to infect humans. A successful zoonotic pathogen must replicate within humans and also be transmitted. How diversity in host immune genes across species impact upon how successfully a pathogen becomes zoonotic poorly understood¹. There are important differences in the innate immune gene repertoires of birds compared to humans. Birds carry many zoonotic pathogens, surprisingly even more than bats, and we have shown that differences in their innate immune genes may contribute to their ability to carry zoonotic infections. This is particularly important at the moment where there is a high burden of bird flu globally. The bird innate immune system is particularly interesting because it is more closely related to ancient animals like dinosaurs. Birds carry a number of zoonotic pathogens and the diversity in the bird gene immune repertoire, compared to humans is profound. Some birds are highly susceptible to bird flu whereas others are not. Understanding the immune differences between bird:bird and bird:human in their responses to flu and other zoonotic pathogens will inform novel strategies for potential therapeutic intervention against viral and bacterial infections. In this project we will investigate how proteins from the innate immune system from humans and animals diverge. We will determine the impact of these genetic differences on the responses of human and animal cell lines to infection. To do this will use CRISPR/Cas9 gene editing to remove or modify innate immune genes in human and animal cells to determine the functional consequences for the evolution of sensing of zoonotic pathogens.

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 and animal cell lines to remove or modify innate immune genes
- Analytical techniques including imaging, FACs, ELISA, PCR and western blot analysis.
- Writing, presentation and literature analysis techniques

References:

¹ <https://www.cam.ac.uk/research/news/farmed-carnivores-may-become-disease-reservoirs-posing-human-health-risk> For further information about the project, please contact Prof Clare Bryant: ceb27@cam.ac.uk

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)