Ref: 10/MG

Project Title: Comparison of quality and dynamics of anti-BTV immunoglobulin subclasses in BTV infected and/or vaccinated cattle and/or sheep.

Supervisors: Marc Guimera, Karin Darpel **Research group:** Orbivirus Research

Project Summary:

Bluetongue virus (BTV) is a pathogen of ruminants (including sheep, cattle, goats and deer) which is transmitted by *Culicoides* biting midges. Whilst BTV is known to cause significant clinical disease in sheep, the disease is typically milder or even asymptomatic in cattle. The serological immune response of ruminants to BTV infection has been poorly explored and assumed to be the same across its ruminant hosts despite clear differences in the clinical disease observed in sheep versus cattle. The only commercial BTV serological assay currently available detects antibodies against the BTV group-specific viral protein, VP7, however can only confirm prior exposure to either BTV infection or vaccination. The detection of these anti-VP7 antibodies does not offer any information on how long ago the animal was infected/ vaccinated, cannot distinguish between infected or vaccinated individuals or if the animal will be protected from re-infection. Therefore new serological assays are required to investigate additional immune response parameters which will enable improvement to future BTV vaccine development and implementation of disease control measures in the field during BTV outbreaks.
In this project we propose to advance the current knowledge of ruminant anti-BTV immune responses and investigate the following hypothesis: "Antibody isotype dynamics and quality against several BTV proteins differ between BTV-infected and vaccinated sheep and cattle".

Details:

The student will initially be involved in generating recombinant BTV proteins, thereby acquiring technical know-how in cloning, protein expression and purification. Recombinant BTV proteins will then provide the basis to develop new serological assays to determine specific serological parameters across available time-course sera obtained from BTV-infected or vaccinated cattle and sheep.
Firstly, the candidate will develop enzyme-linked immunosorbent assays (ELISAs) detecting specific antibody subclasses (IgM, IgG(Fc), IgG1 and IgG2) against selected BTV proteins. Preliminary results based on the commercial VP7 ELISA platform have demonstrated the feasibility of isotype-specific anti-BTV ELISAs. The project will compare different ELISA formats (indirect, competitive, sandwich) to identify the assay type offering the best signal-to-noise performance.
The generated BTV proteins will further be used to develop avidity assays to characterise the specific epitope binding quality of anti-BTV antibodies comparably across sheep and cattle sera post infection and/or vaccination. The student will have the opportunity to investigate correlation of the identified antibody dynamics and quality to virological parameters of BTV infection of sheep and cattle (using real-time RT-PCR, virus titration and/or isolation) and detailed data analysis and statistical modelling depending on interest.
Overall, the project offers excellent opportunities to develop technical competence in key scientific technologies across molecular biology, immunology and diagnostic assay development, while investigating an exciting research hypothesis.
The student will join the Orbivirus Research group, whose main interest is the study of host-virus-insect vector interactions of *Culicoides*-borne viruses. All the necessary training, including how to work in high containment, will be provided within the group and the Institute. The candidate will be directly supervised by a postdoctoral scientist employed on a DEFRA science project in this area, while having the full support of all group members to guarantee strong technical support of the student across all aspects of the project.

References for Suggested Reading:

- Melzi E et.al. Follicular dendritic cell disruption as a novel mechanism of virus-induced immunosuppression. Proc Natl Acad Sci U S A. 2016 Oct 11;113(41):E6238-E6247
- Bréard E et.al. 2019 Evaluation of an IGM-specific ELISA for early detection of bluetongue virus infections in domestic ruminants sera. Transbound Emerg Dis. 2019 Jan;66(1):537-545
- Maclachlan NJ et.al. The pathology and pathogenesis of bluetongue. J Comp Pathol. 2009 Jul;141(1):1-16
- Maclachlan NJ et.al. The immune response of ruminant livestock to bluetongue virus: from type I interferon to antibody. Virus Res. 2014 Mar;182:71-7

To Apply:
Please email your CV (no more than two sides of A4) and a covering letter detailing why you would like to undertake the placement and the knowledge and skills that you will bring to the Institute to yvonne.walsh@pirbright.ac.uk.
Closing date to apply: 31.01.20