Reference: 09/AY

Project Title: Development of a novel opsonisation assay to investigate the role of non-neutralising antibodies in FMDV immunity

Supervisors: Dr Amina Yasmin, Dr Andrew Shaw Research group: Picornavirus Molecular Biology

Project Summary: Foot-and-mouth disease virus (FMDV) is a highly contagious disease of cloven-hoofed animals such as cattle, sheep and pigs and maintenance of a country's FMD free status is critical for the free trade of animals and animal products. Research has shown that the antibodies which develop following vaccination of animals play a major role in providing protection against FMDV.

Antibodies can be categorised as either neutralising or non-neutralising. Neutralising antibodies confer protection by directly preventing viruses from infecting new host cells. In contrast, non-neutralising antibodies provide protection via various 'effector functions' mediated by the constant fragment crystallizable (Fc) portion of the antibody. Opsonisation is a process whereby the formation of immune complexes between pathogens and antibodies enhances the ability of phagocytic cells to take up and destroy pathogens. Understanding the role of antibodies in Fc-mediated opsonisation in the immune response to FMDV can highlight important parameters to consider during FMDV vaccine design strategies.

In this project the student will investigate the ability of FMDV-specific antibodies to mediate the opsonisation process. This project builds upon some initial observations and will further our knowledge regarding the contribution of specific subsets of antibodies with respect to their role in protection against infection.

Further Details: Previously our group has shown that non-neutralising mouse monoclonal antibodies (mAbs) directed against the surface of the FMDV particle can form an immune complex with FMDV capable of inducing Fc-mediated uptake into both a mouse macrophage derived cell line (RAW264.7) expressing the immunoglobulin G (IgG) Fc receptor II (Fcγ RII), and cow monocyte-derived macrophages. Importantly, these macrophage cells only become susceptible to FMDV infection when the virus forms an immune complex. These preliminary findings suggest Fc-mediated antiviral functions of antibodies associated with entirely conserved non-neutralising epitopes may provide novel approaches for inducing broadly effective protective responses.

In this project, the student will confirm and expand upon these preliminary results by investigating a diverse collection of broadly cross-reactive, non-neutralising mAbs and their ability to mediate Fc-dependent opsonization. The student will also get the opportunity to characterise antigen-antibody affinity for non-neutralizing and neutralizing antibodies and correlate this with Fc-mediated function.

This project will also further investigate the presence of opsonizing antibodies within polyclonal sera collected from vaccinated cattle. Using the experience gained working with mAbs, this second part of the project will be driven more by the student. The project will first use the control serum in order to adapt and standardise the opsonisation assay. Once established, the assay will be used to assess the presence of opsonising antibodies within polyclonal serum derived from vaccinated and/or challenged animals. The results from the opsonisation test will then be compared to the corresponding data from the established "gold standard" virus neutralization test (VNT), an assay that is widely used to detect antibodies that can neutralise virus infection.

References for Suggested Reading:

Robinson L, Windsor M, McLaughlin K, Hope J, Jackson T, Charleston B. Foot-and-mouth disease virus exhibits an altered tropism in the presence of specific immunoglobulins, enabling productive infection and killing of dendritic cells. J Virol. 2011 Mar;85(5):2212-23.

McCullough KC, Parkinson D, Crowther JR. Opsonization-enhanced phagocytosis of foot-and-mouth disease virus. Immunology. 1988;65(2):187-191.

Baxt B, Mason PW. Foot-and-mouth disease virus undergoes restricted replication in macrophage cell cultures following Fc receptor-mediated adsorption. Virology. 1995 Mar 10;207(2):503-9.

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 studentship@pirbright.ac.uk.

Closing date to apply: 09.00, 7th February 2022