Project Title: Improvement of HVT vector platform by knockout of the non-essential HVT genes using CRISPR/Cas9 system

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Research Group: Viral Oncogenesis Group

Project Summary: Herpesvirus of Turkey (HVT) has been successfully used as a vaccine to protect chickens against Marek’s disease for decades. HVT is also one of the most successful and widely used viral vectors for generation of recombinant vaccines that deliver protective antigens of other avian pathogens. To overcome the interference between individual recombinant HVT vaccines, we have developed multivalent HVT vectored vaccines capable of inducing simultaneous protection against multiple avian pathogens. However, the animal experiments using the triple-insert HVT vectored vaccines we developed showed reduced replication efficiency in chickens, indicating that the insertion of foreign genes affects HVT replication in vivo. It also suggested that the HVT may not be able to express more than 3 cassettes without compromising on replication thus limiting the induction of immunity. The aim of this project is to explore the hypothesis that knocking out the non-essential genes in the HVT vector can enhance replication enabling recombinant HVT-based vaccines to induce stronger immune responses.

Further Details: We have developed a CRISPR/Cas9-based gene editing pipeline to identify essential/non-essential genes of HVT. Essential nature of each gene can be identified from the replication visualised by the specific plaques in cell culture in comparison to the parental virus. Based on the screening results, we aim to develop a ‘minimal essential’ recombinant HVT vector deleted in most of the non-essential genes for further in vivo replication and efficacy studies. The student will explore the following avenues:

1. Knockout of the individual non-essential genes in HVT-ND-IBD-ILT using the established pipeline to generate the mutant viruses. In this part of the work, the student will learn the technique on the generation of mutant virus by CRISPR/Cas9 editing.

2. Determine the in vitro replication of mutant viruses. The student will compare the growth of the mutant virus with the parental virus which involves the titration of virus stock and producing growth curve of mutant viruses using the established protocol.


References for Suggested Reading:


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