

Reference: 04/BH

## Project: Correlates of influenza transmission

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Research Group: Swine Influenza Immunology

### Project Summary:

The recent human pandemic in 2009 has emphasised the need to understand the biology of the influenza viruses that transmit between humans and pigs. During the pandemic in 2009, fear that pig viruses may infect people resulted in the widespread destruction of animals and trade bans caused economic losses to the US industry of <\$1 billion. More informed management of pigs during human influenza virus epidemics requires more detailed understanding of virus transmission dynamics and the effects of transmission and vaccination on viral evolution. We have performed 12 controlled one to one transmission experiments in pigs in which donor infected animals were exposed to naïve recipients at different times to determine the period of infectiousness, the latent and incubation period for influenza virus infection. We have systematically collected samples from the upper respiratory tract and blood from these donor and recipient animals to identify correlates of transmission.

### Details:

The understanding of the dynamics of disease transmission is of key importance for the adequate design of effective control measures. We have performed a unique set of transmission one to one experiments. Four replicate nasal swabs samples were taken for virus isolation, quantification of virus genome and host gene expression. Blood samples were also collected every day to monitor antibody titres and the presence of cytokines. The overarching aim of this proposal is to identify correlates of transmission of pandemic H1N1 virus. This will be addressed through the following specific objectives:

#### **Objective 1. Identification of virological and immunological correlates of transmission**

The student will isolate RNA from the nasal swab samples and perform qPCR to identify viral load. This will be correlated with live virus determined by plaque assays. No information is available on the correlation between qPCR and plaque detection of virus in such a large dataset and therefore this will be novel data. In addition the RNA isolated from NS and blood will be analysed for innate immune genes using the Fluidigm system in collaboration with Kerstin Skovgaard in Copenhagen. Genes of interest expressed at the time of transmission will be verified using qPCR or by ELISA. In addition cytokine profiles in serum and nasal fluid will be determined by Luminex cytokine assays. All this information will be analysed by mathematical modelling in collaboration with colleagues at Edinburgh University to establish correlates of transmission.

**Objective 2. Validation of signatures of transmission in immunized animals.** The student will be able to take ownership of the project by extending the analysis of particular signatures or genes identified. We have a huge bank of NS, serum and BAL samples from many experiments from protected immunised or infected animals at different times post infection. The student will establish whether immunized and challenged animals show signatures of transmission.

The successful applicant will acquire a broad background in immunology, virology and molecular biology. The student will have the opportunity to attend the diverse seminar programme at the Pirbright Institute, take part in journal clubs and to present their work at lab meetings.

### References for Suggested Reading:

- Pandemic influenza. Straight from the pig's mouth: swine research with swine influenzas. Cohen J. Science. 2009 Jul 10;325(5937):140-1.
- Harnessing Local Immunity for an Effective Universal Swine Influenza Vaccine. Tchilian E, Holzer B. Viruses. 2017 May 5;9(5).