# Department of Veterinary Medicine

Available PhD Project:

**Supervisor:**            Dr Lucy Weinert
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**Project Title:**    **Why might bacterial pathogens have small genomes?**

**Description**: In an increasingly post-antibiotic era, creative approaches to combating infectious disease are becoming paramount. This projects aims to understand why and how bacteria become pathogens. Identifying common features of pathogen emergence - whether they be repeated genomic changes or shared epidemiological contexts - would give us predictive power. This might allow us to forecast pathogen emergence, to develop preventative strategies, or improve treatments.  One promising phenomenon to study in this context is the link between reductive genome evolution and pathogenicity. Bacterial pathogens very often have smaller genomes and fewer genes than their nearest non-pathogenic relatives. This pattern applies in phyla as diverse as the Firmicutes, Tenericutes and Proteobacteria, and applies to some of our biggest threats, such as the causative agents of dysentery and tuberculosis.    However, despite much speculation, it remains unclear why this pattern holds. *Streptococcus suis*, a bacterium that is common in non-pathogenic forms, but which also causes serious diseases in pigs and humans is an ideal system in which to investigate this question. Preliminary data show that S. suis has made several recent and independent transitions to pathogenicity, each associated with genome reduction, and that the gene loss is non-random, suggesting that the process might be predictable.

Using hundreds of samples of whole genomes from global *S. suis* populations, this project will produce the first large-scale tests of the various hypotheses linking genome reduction and pathogenicity using functional data and statistical approaches.    The hypotheses can be classified in to two main types. Some authors have argued that reduced genome size is a direct cause of pathogenicity. Other authors, by contrast, have argued that reductive genome evolution follows after pathogenicity, as a passive by-product of adopting that lifestyle.    Discriminating between these competing hypotheses is important for understanding the emergence of pathogenicity, and might also have direct implications for treatment strategy. For example, if reduced population size predictably leads to pathogenicity, prophylactic treatments with incomplete bacterial suppression could be worse than no treatment at all.

Central to the role will be compiling and testing these competing hypotheses about reductive evolution and pathogenicity, such as using phylogenetic methods to understand the rates of gene loss events and compiling genes in to different functional categories and testing their loss rates against control sets. Some of these hypotheses may even be tested in the lab by understanding how extra-chromosomal DNA affects the ability of pathogens to function.  This project will also determine new potential vaccine candidates by identifying the genes that buck-the-trend of genome reduction.  Together, the proposed research will further our understanding of an important emerging pathogen, and of pathogenicity much more broadly.

This project is expected to be part laboratory based and part computational. The student will learn skills in:
•**Genomics**    • **Evolutionary Biology**    • **Bioinformatics**    • **Molecular Biology**    • **Systems Biology**    • **Statistics**

References
Weinert *et al*. (2015) Genomic signatures of human and animal disease in the zoonotic pathogen *Streptococcus suis*. *Nature Communications* 6: 7640

Albalat & Cañestro (2016) Evolution by gene loss. *Nature Reviews Genetics* 17, 379–391

Toft & Andersson (2010) Evolutionary microbial genomics: insights into bacterial host adaptation. *Nature Reviews Genetics,* 11, 465-475

**Funding:**
This project is not funded.  Prospective students would be expected to apply for funding opportunities either through the University (http://www.vet.cam.ac.uk/grad/Prospectivestudents/funding) or other sources.

**How to apply:**  Contact the Supervisor to discuss before submitting an application.
More details on how to apply here: http://www.vet.cam.ac.uk/grad/Prospectivestudents/apply