

## PhD Project: Investigating pathogenicity in zoonotic *Streptococcus suis*

Supervisor: [Dr Lucy Weinert](#)

Co-supervisors: Prof Jerry Wells, Dr Dan Tucker

### Project Description

This project offers an exciting opportunity to join a large European consortia and make a tangible impact on a global animal and human health issue. You will investigate the major swine and zoonotic pathogen, *Streptococcus suis*, a bacterium responsible for significant mortality in pigs and severe infections in humans. The rise of antibiotic resistance and a lack of effective, cross-protective vaccines pose a serious challenge to animal welfare and public health.

Recent genomic analysis of over 3,000 *S. suis* isolates by our group has uncovered that most disease cases are caused by a small number of highly virulent lineages (Murray *et al.* 2024 *PNAS*). These lineages originated during intensification of pigs and their emergence coincided with the acquisition of three specific pathogenicity-associated islands (PAIs). These PAIs were acquired through horizontal gene transfer, and their surface proteins are highly conserved across the most problematic pathogenic lineages. This project will build on this discovery to inform novel strategies for disease prevention.

### Project Objectives and Work Plan

The primary objective is to elucidate the function of two of these three PAIs to identify new targets for cross-protective vaccines and immune exclusion strategies. This PhD will involve a combination of molecular biology, biochemistry, and bioinformatics.

- **Functional Analysis of PAI-3:** You will purify a large cell-wall anchored glycosidase encoded by PAI-3, which we hypothesise is crucial for nutrient acquisition and colonisation by breaking down host sugars. You will test its enzymatic activity and study the role of a co-encoded ABC transporter in nutrient uptake. You will also use RNA sequencing (RNA-seq) to identify genes regulated by a sugar-sensing repressor, providing a deeper understanding of this system's role in host interaction.
- **Functional Analysis of PAI-2:** You will investigate the role of a pilus assembly system encoded by PAI-2. Pili are hair-like appendages that we hypothesise are involved in adhesion, biofilm formation, and evading the host immune system. You will generate specific antisera against the pilin subunit and use advanced microscopy and flow-cell models to study microcolony and biofilm formation. This work will also assess the pilin's role in adhesion to pig tonsil tissue and its contribution to antibiotic tolerance.
- **Protein Expression and Purification:** A key part of the project will involve the practical work of expressing and purifying the major pilin subunit from PAI-2 and the glycosidase from PAI-3. This work will not only enable the functional studies in WPs 1 and 2 but will also generate the proteins needed for future vaccine development research.

This project will make a significant contribution to tackling a major global health challenge. You will receive extensive training in cutting-edge genomic, proteomic, and microbiological techniques. The project combines fundamental research with a clear pathway to practical applications, addressing a critical need for new solutions in veterinary and human medicine.

**Funding:** Full funding is available for the successful applicant eligible for the home fee rate.

**How to apply:** Contact the Supervisor to discuss the project before submitting an official application. More info on applying here: <https://www.postgraduate.study.cam.ac.uk/courses/directory/cvvtmrvet>