FoodBioSystems DTP - PhD Project Advertisement

Project title: FBS2021-16-McCarthy: Improving livestock resilience by understanding the role of the microbiome in viral infection progression and antibiotic resistance

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Project description:
The microbiome in humans has been well studied and has been shown to influence important physical functions such as energy metabolism and immune system development (Cani *et al*., 2018). Compared to humans relatively little is known about the role of the gut microbiota in pigs This is despite a number of studies linking the pig microbiome to average daily weight gain, feed efficiency, feed conversion, feed intake and to its capacity to act as a reservoir for antibiotic resistance genes (McCormack *et al.,* 2020, Wang *et al.,* 2019, Ghanbari *et al.,* 2019). This project aims to investigate the impact the viral infection has on the gut microbiome and the resistome (all the genes associated with conferring antibiotic resistance within the microbiome). It has two specific objectives:

1. **Uncover the role of the microbiome in viral infection:** This aim will involve profiling the microbiome of a healthy cohort of pigs and comparing it to that of animals infected with commercially relevant porcine viruses.

a. *Porcine reproductive and respiratory syndrome virus (***PRRSV)**: PRRSV is a porcine pathogen that causes respiratory disease in young pigs and reproductive failure in breeding stock. It is estimated to cost the EU Agricultural sector 1.5 billion euros each year and for the global protein production is the biggest threat to food security next to African swine fever (that has killed an estimated 60% of pigs in China over the last two years) (Salguero *et al.,* 2015). This project extract gDNA from the fecal matter of pigs infected with PRRSV and non-infected pigs. In house next generation sequencing (Illumina iSeq, Oxford Nanopore Minion) will be used to profile the impact of PRRSV infection on the gut microbiome.

Figure 1: Project Outline: This project aims to explore 1) the impact on viral infection on the gut microbiome 2) the impact of viral infection on the resistome

b. **Classical Swine Fever Virus** (CSFV): CSFV is an economically significant, multi-systemic, highly contagious viral disease of pigs worldwide (McCarthy *et al.,* 2019). The disease is exotic to the UK and thus notifiable, but the APHA has a continuous threat-mitigation related research programme. Currently there are no studies exploring the impact of CSFV on the gut microbiome of pigs. This study will sample fecal matter from animals infected with CSFV and control animals. Similarly, to the PRRSV study, the microbiome of these two cohorts will be interrogated.

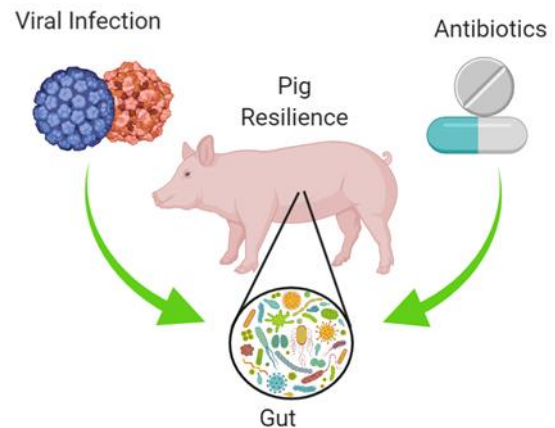c. **Antiviral Probiotics:** The fluctuations in diversity, richness and specific species composition within the

microbiomes from both of these studies will be compared to each other and to other publicly available microbiome datasets, to identify common bacterial strains that are typically depleted during viral infection. The impact that these strains have on viral replication will then be explored *in vitro* by assessing the impact of these bacteria on viral replication.

2) **Investigating the link between viral infection and the Resistome:** Antibiotic resistance is one of the greatest threats to global healthcare systems (McCarthy *et al.,* 2019). Antimicrobials are widely used for disease prevention and growth promotion in pigs. In fact, 80% of antibiotic use in the US is in agriculture (Boeckel *et al.,* 2015). The One Health perspective has been critical in demonstrating the role antibiotic misuse in agriculture has in perpetuating the current antibiotic resistance crisis in hospitals (Manyi- Loh *et al.,* 2018). In this aim, we will explore how viral infection impacts the prevalence of Antibiotic Resistance Genes (ARGs) within the gut microbiome of pigs.

a) *In silico* analysis of WGS data from published swine microbiomes to identify antibiotic resistance genes and their prevalence.
b) Targeted ARG Amplicon Enrichment and Sequencing from CSFV and PRRSV Study.
c) Analysis of prevalence of ARGs in microbiomes of animals pre and post infection with CSFV and PRRSV.
d) Determine what ARG enrichments or depletions are specific to CSFV and PRRSV

The understanding of the porcine gut microbiome during viral infection that will come from this study will provide an opportunity to improve swine health and welfare, minimize the economic losses to producers associated with viral infections, and lessen the risk of antimicrobial resistance in pigs.

Training opportunities:
The student will have an opportunity to involved in animal studies at our partner in the Animal and Plant Health Agency

Student profile:
We particularly encourage applicants with a first class/upper second class honours degree and / MSc in Microbiology or a closely related subject and students with a strong interest in microbial genomics.

Funding Note
This project is part of the FoodBioSystems BBSRC Doctoral Training Partnership (DTP), it will be funded subject to a competition to identify the strongest applicants.
The studentship is open to UK and international students (including EU countries) however due to funding rules, no more than 30% of the projects can be allocated to international students.
The funding will include a tax free stipend (minimum £15, 285 per year), support for tuition fees at the standard UK rate (currently £4,407 per year) and a contribution towards research costs. **Please note** that the host universities have not yet confirmed the level of fees charged to international students funded by the DTP. Fee levels may vary across the institutions. This information will be shared on the FoodBioSystems DTP website as soon as it becomes available.

To apply
Please go to FoodBioSystems DTP website for information on how to apply for this studentship. The closing date for applications will be 8 February 2021.