FoodBioSystems DTP - PhD Project Advertisement

Project title:
FBS2021-54-Lewis: The developing gut microbiota and immune system: Iron and zinc – friend or foe?

Lead supervisor:
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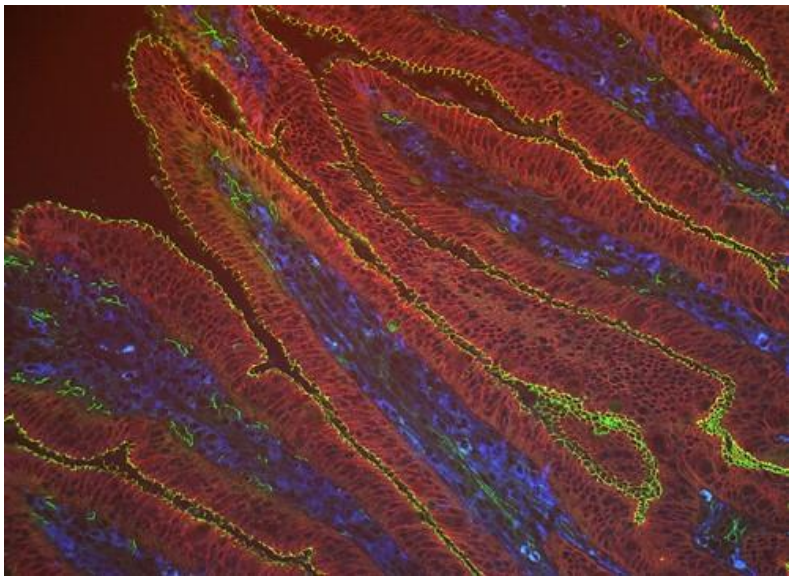
Project description:
Under normal conditions, the pre-weaned gut is largely iron-free since breastmilk contains only limited iron. However, the sudden introduction of oral iron at weaning generates an iron-rich gut environment. This promotes the growth of pathogenic microbial populations in the gut with high-iron requirements whilst disadvantaging beneficial bacteria that have low-iron requirements. This is likely to skew the pattern of microbial colonisation of the gut during a critical phase of development. Since gut microbes are the primary drivers of immune development, changes to these populations during early life is likely to change how the immune system develops and combats infectious disease. We do not have clear understanding of how luminal iron availability affects microbiota development, or subsequent immunity.

To reduce pathogen-induced infant diarrhoea in low-income countries, diets are often supplemented with high levels of zinc oxide (ZnO). This is because it has antimicrobial properties leading to reductions in pathogen growth and colonisation of the gut. However, since genes encoding antibiotic resistance and genes encoding zinc resistance often occur on the same plasmids, ZnO could actively promote the generation of antibiotic resistant microbes by selecting for these plasmids. The mechanisms of ZnO actions are unknown making it difficult to develop alternatives which do not promote antibiotic resistance.

We hypothesis that ZnO reduces enteric infection during infancy by inhibiting microbial iron uptake and reducing pathogenic expansion and virulence in the gut. Low-iron diets could reduce enteropathogen growth and thus negate the need for ZnO.

Piglets are valuable models for nutrition studies since they share many characteristics of gut physiology, immunity, microbiota and diet with humans. Specific to this study, piglets are born with very low iron reserves and quickly develop iron deficiency anaemia. This means iron levels can be tightly controlled making piglets valuable models to study the negative effects of oral iron supplementation.

The aim of this study is to determine whether limiting luminal iron during infancy reduces enteropathogenic growth and therefore provides a simple, yet effective, alternative to ZnO, thus reducing levels of antibiotic resistant microbes in the gut. It will also explore whether patterns of both microbiota and immune development return to normal in the absence of iron and zinc using a piglet model for human infants. It then explores alternative methods of iron supplementation which do not flood the gut with iron during a critical phase of development for both the gut microbiota and immune system.



Training opportunities:

Specific training will be provided in analytic techniques including

- Microscopy (4-colour quantitative immunofluorescence)
- Microbiota population analysis (high throughput sequencing, fluorescent *in situ* hybridization coupled with flow cytometry).
- Shotgun metagenomics
- *in vitro* gut modelling
- Metabolic profiling (NMR spectroscopy, gas chromatography/mass spectroscopy)
- Statistical techniques in handling large datasets

Since this PhD project is in partnership with the University of Surrey, there will be additional valuable opportunities for gaining experience in veterinary microbiology.

Student profile:

Due to the multidisciplinary nature of this program, we do not expect the successful candidate to have knowledge and experience in all relevant areas. However, we do expect the appointed to have a background in immunology, metabolism, microbiology nutrition and/or gut health (or other appropriate subject) preferably, but not necessarily, to MSc level. Full support and training will be provided by experienced staff.

References:

https://www.cell.com/med/pdf/S2666-6340(20)30021-0.pdf

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.