

Clone wars in niche space: exploring the evolutionary and genetic basis for bacterial species

Supervisory team:

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Project description:

Understanding the forces that shape bacterial genetic variation is a fundamental problem in microbiology. Classifying bacteria into meaningful species groups is also essential for applied microbiology and ecology. Many bacterial species have been shown to exhibit extensive variation in gene repertoires, where a set of core genes shared by all strains are supplemented with a set of accessory genes that are only present in a subset of strains. The ability to exploit particular niches is thought to depend on the acquisition of a range of accessory genes, typically acquired via horizontal gene transfer (Vos et al. 2015). However, genetic variation in core genes shared between different strains is often associated with ecological niche (Raymond et al 2010, Zheng et al 2017)(Figure 1), suggesting that variation in core genes may be ecologically significant.

This project will explore the extent to which core genetic variation arises from neutral genetic drift process and from positive selection in distinct habitats, a question with broad importance for understanding bacterial biology and evolution. For instance, many isolates of economic and therapeutic importance (*Bacillus thuringiensis* biopesticides, *Escherichia coli* probiotics etc) are closely related to isolates capable of causing disease. In both these cases, humans consume large doses of viable microbes in food or as therapeutic agents. Understanding the potential of beneficial bacteria to cause harm or acquire harmful genes is particularly important for assessing the safety of these uses. If core genetic variation limits virulence or niche shifts then the risk of these applications will be substantially reduced (Raymond & Federici 2017). *Bacillus thuringiensis*, in particular, has an excellent safety record and is the most widely applied microbial insecticide, facilitating environmentally friendly mosquito control and pest management. Nevertheless, disagreements regarding its ecological niche, and its taxonomic status relative to *Bacillus cereus*, a causative agent of diarrhea, have threatened its continued use in the European Union. In this project, the student will (1) carry out genome sequencing and phenotypic characterization of isolates from natural populations (2) apply experimental evolution and re-sequencing approaches to look for convergent adaptive mutations in novel niches (3) use CRISPR-Cas9 genome editing to introduce putative adaptive alleles into different genetic backgrounds. This project will be lead by Dr Ben Raymond & Dr Michiel Vos at the University of Exeter and co-supervised by Prof Sam Sheppard at the University of Bath. Dr Raymond has worked on *Bacillus thuringiensis* and its relatives for more than 15 years. Michiel Vos has a longstanding interest in bacterial recombination and genome evolution. Prof Sam Sheppard leads a population genomics group at the University of Bath.

References. Raymond, B., & Federici, B.A. (2017). FEMS Microbiology and Ecology. doi: 10.1093/femsec/fix084 Zheng, J., Gao, Q., Liu, L., Liu, H., Wang, Y., Peng, D., Ruan, L., Raymond, B., & Sun., M. (2017) mBio 8:e 00822-17. doi: 10.1128/mBio.00822-17. Raymond, B., Wyres, K., Sheppard, S., Ellis, R.J., Wright, D.J., & Bonsall, M.B (2010). PLoS Pathogens 6(5): e1000905. Vos, M., Hesselman, M., Te Beek, T., van Passel, M., Eyre-Walker, A. (2015) Trends Microbiol 23.10: 598-605

Figure 1. The core genome based phylogeny of the *Bacillus cereus* group shows several genetically distinct clusters that are associated with particular niches. Clade 1 contains *Bacillus anthracis*, the causative agent of anthrax, and the majority of the severe vertebrate adapted pathogens. Clade 2 contains the majority of the isolates carrying insecticidal toxins (in green) and all isolates used as biological pesticides. Clade 3 is strongly associated with the rhizosphere; strains in this clade have far fewer virulence genes. The long branch lengths between clades indicate the large number of genetic changes in core genes that separate these clades (see Raymond & Federici 2017 FEMS Microbiol Ecol, doi: 10.1093/femsec/x084).

