Gemma Murray, Newnham College, Research Fellowship Report

My research aims at understanding how and why bacteria evolve to cause disease in their hosts, and how antibiotic resistance is acquired and maintained in bacterial populations. To address these questions, I analyse diversity within natural populations, using methods that combine comparative genomics, population genetics, epidemiology and microbiology. My research focusses on two opportunistic bacterial pathogens: *Streptococcus suis* and *Staphylococcus aureus*.

Streptococcus suis is carried on the tonsil of all pigs, and can lead to severe respiratory and systemic infections. It has a significant impact on animal welfare and antimicrobial usage in farming, and can also cause severe infections in humans. My work on *S. suis* has involved collaboration with two research programs: the Myanmar Pig Partnership program and the Horizon 2020 Program for Innovative Global prevention of *S. suis*. These collaborations have allowed me to work on several projects that aim at reducing the global impact of *S. suis* on both farming and public health. I have contributed to the development of a diagnostic test for pathogenic strains of *S. suis*, and the development of a vaccine. I have also led projects that have used the natural diversity within *S. suis* to investigate two correlates of the evolution of pathogenicity: genome size and mutation rate. Both of these associations help us to understand the adaptive potential of pathogens, and could help us target populations that are more likely to cause disease.

Genome size
I worked on the first systematic study of the association between a reduction in genome size and pathogenicity in bacteria. Our results revealed that genome reduction, including the loss of genes, is associated with the evolution pathogenicity over a broad taxonomic, ecological and temporal range. This work was published last year in *Molecular Biology and Evolution*.

Mutation rate
While it is thought that mutation rates are generally held as low as possible, higher rates may sometimes be an advantage. They may particularly benefit bacterial pathogens, that have to infect new hosts, grow in challenging environments, and evade host immunity. I worked on a study that was the first to demonstrate an association between a pathogenic ecology and mutation rate. This work is currently under review, but is available as a pre-print on *BioRxiv*.

I have also been involved in assembling a large global collection of *S. suis* genome sequences, which I have used to understand specific genomic changes that have accompanied the evolution of pathogenicity. I have identified several mobile genetic elements associated with increased pathogenicity, and am working with collaborators to functionally characterise them. This work could help us to understand the constraints on the evolution of pathogenicity, and how frequently novel pathogenic strains may emerge.

My work on *Staphylococcus aureus* has focused on understanding the success of the most common *S. aureus* lineage in European livestock. *S. aureus* is a common component of the human nasal and skin microbiomes, and an important cause of antibiotic-resistant infections. *S. aureus* also colonises a wide range of domestic and wild animal species. I have worked with a PhD student over the last year to understand the evolution of antibiotic resistance and changing host-association of the dominant livestock-associated *S. aureus* lineage in Europe. This work helps us to understand the risks livestock-associated pathogens pose to human health.

Papers

Published:

Murray GGR, Charlesworth J, Miller EL, Casey MJ, Lloyd CT, Gottschalk M, Tucker AW, Welch JJ & Weinert LA. 2020. Genome reduction is associated with bacterial pathogenicity across different scales of temporal and ecological divergence. *Molecular Biology and Evolution* 28(4).

Funck J, Heintzman PD, Murray GGR, Shapiro B, McKinney H, Bigelow N, Huchet J-B, Druckenmiller P, Wooller KJ. 2020. A detailed life history of a Pleistocene steppe bison (*Bison priscus*) skeleton unearthed in Arctic Alaska. *Quaternary Science Reviews* 249;106578.

Dehasque M, Ávila-Arcos MC, Díez-del-Molino D, Fumagalli M, Guschanski K, Lorenzen ED, Malaspinas A-S, Marques-Bonet T, Martin MD, Murray GGR, Papadopulos AST, Therkildsen NO, Wegmann D, Dalén L, Foote AD. 2020. Inference of natural selection from ancient DNA. *Evolution Letters* 4(2).

Matuszewska M**,** Murray GGR, Harrison EM, Holmes MA & Weinert LA. 2020. The evolutionary genomics of host specificity in *Staphylococcus aureus*. *Trends in Microbiology* 28(6).

Under review:

Murray GGR, Balmer A, Herbert J, Hadjirin N, Kemp C, Matuszewska M, Bruchmann S, Gottschalk M, Tucker AW, Miller EL & Weinert LA. Mutation rate dynamics reflect ecological changes in an emerging zoonotic pathogen. Preprint available on *BioRxiv*.

Conference and meeting presentations

The evolution of pathogenicity in *Streptococcus suis*. Departmental Seminar, Department of Veterinary Medicine, University of Cambridge. March 2021

Population structure and pathogenicity of *Streptococcus suis*. PIGSs,General Assembly Meeting, February 2021

The relationship between mutation rate, genome size and pathogenicity in *Streptococcus suis*. Population Genetics Group Meeting, Leicester, January 2020

Teaching

Part II Pathology, one lecture – Introduction to molecular epidemiology (2019/2020 & 2020/2021)

Part II Genetics, two lectures – Introduction to phylogenetics and molecular epidemiology (2019/2020)