**University of Leicester**

**BBSRC MIBTP Studentship Project 2025-6 entry.**

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**Section 2 – *Project Information***

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| **Project Title** | Understanding within-host genetic diversity and evolution of human-associated bacteria  |
| **Project Summary**  |
| Evolution of major bacterial pathogens poses great risks for their hosts as it potentially allows better adapted, more virulent and/or more resistant variants to emerge. On the other hand, a multitude of studies highlight that bacteria in general play a large role in shaping the health and metabolism of their hosts through microbiotic interactions. Thus, understanding the evolution of commensal, opportunistic and virulent bacteria within human and other hosts is key to allow for targeted interventions to shape a healthy within-host bacterial interaction.  However, these systems are complex and not fully understood. Especially the effect of within-host evolution on the species-wide evolution is far from clear. This microevolution process typically starts with the transmission of a few bacteria from a donor host, followed by population expansion in the new host. This allows the rise of new mutations and the acquisition of foreign DNA segments via horizontal gene transfer (also called bacterial recombination), including adaptive variants that can rapidly fix in the new population.  The study of within-host evolution has had a slow start in part due to the lack of knowledge on whether many of the sophisticated analysis methods available to infer population history and the processes shaping the genetic diversity of between-host microbe populations are also applicable for within-host microbe populations. The main aim of this project is to understand how within-host population history, selection, mutation and recombination rates shape within-host genetic variation of human-associated bacteria.   For this (objective 1), you will build synthetic genomes using parameters of above-mentioned evolutionary processes described in the scientific literature using a state-of-the-art simulation tool [1], and evaluate and compare resulting genetic variation.   Then (objective 2), you will feed your synthetic genomes into population genetics tools commonly used for inference of between-host (populational) evolution and evaluate if these tools can infer the within-host evolutionary model that you considered originally. This will lead to a best-practice guide of how to perform within-host evolution inference.   Finally (objective 3), you will then apply your optimised pipelines to analyse  within-host genetic variation and evolution of public and in-house available real-world genomic datasets of Heliobacter pylori and  Streptococcus pneumoniae [2].   Techniques that will be undertaken during the projectThis project provides an opportunity to learn and apply state-of the-art computational, population genetics and evolution, and machine learning approaches. Specifically, you will perform computer simulation of bacterial genomes, use population genomics tools for inferring evolutionary processes such as natural selection and machine learning techniques to fit evolutionary scenarios to real-world genomes that you will assemble and align via genomics techniques.  |
| **References** |
| [1] Cury, J., Haller, B.C., Achaz, G. and Jay, F., 2022. Simulation of bacterial populations with SLiM. Peer Community Journal, 2. doi:10.24072/pcjournal.72  [2] Davison, C., Tallman, S., de Ste-Croix, M., Antonio, M., Oggioni, M.R., Kwambana-Adams, B., Freund, F. and Beleza, S., 2024. Long-term evolution of Streptococcus mitis and Streptococcus pneumoniae leads to higher genetic diversity within rather than between human populations. PLoS genetics, 20, p.e1011317. https://doi.org/10.1371/journal.pgen.1011317  |