PhD Project Proposal: Microbiomics and genetics of human attractiveness to malaria mosquitoes

Research question:

What are the relative contributions of the skin microbiome, genetics and *Plasmodium* infection in human attractiveness to mosquitoes?

Background:

Some people attract mosquitoes more than others due to differences in volatile organic compounds (VOCs) emitted from the human skin (Logan et al. 2008). The production of these volatiles is thought to be mainly influenced by bacteria living on the skin (Takken and Verhulst 2017) as well as genetic differences between people (Fernández-Grandon et al. 2015). However, the mechanisms involved in the production of VOCs and the relative contribution of the skin microbiome and of genetics remain to be investigated.

Attractiveness to biting insects is important in the medical context, since it directly impacts the transmission of parasites by mosquitoes such as *Plasmodium falciparum*, the agent of human malaria. Interestingly, people tend to become more attractive to mosquitoes when infected with *Plasmodium* which could potentially increase the transmission of the parasite to the mosquito vector (Busula et al. 2017). Whether this effect of the infection is mediated by changes in the skin microbiome in infected people, and whether it interacts with the host's genetic factors, is not known.

The project will aim to decipher the respective roles and potential interactions between the skin microbiome, human genetic factors and *Plasmodium* infection on attractiveness to mosquitoes.

Methods:

During the project, I will analyse the skin microbiome composition of participants recruited in the UK from whom attractiveness to malaria-transmitting mosquitoes and skin volatiles have been characterised. I will use molecular biology techniques to extract the bacterial DNA from the samples and prepare them for high-throughput sequencing. Using bioinformatic tools I will analyse the sequences and determine the bacterial diversity present in the samples to measure correlations with the production of VOCs and levels of attractiveness to mosquitoes. I will also test whether the skin microbiome is influenced by genetic factors by making use of the genomic data already available from the participants.

I will also conduct a similar study of the skin microbiome on a natural mosquito-human-*Plasmodium* system. Field work will be carried in Gambia to collect microbiome samples and will also involve volatile collection, chemical analysis of VOCs and behavioural assays using mosquitoes in the lab. The effect of *Plasmodium* parasites will also be tested by checking the infection status of the participants.

Impact:

The findings will help us understand parasite-mosquito-human interactions and their effect on malaria epidemiology. It could also help the development of new ways to prevent mosquito bites and protect human populations at risk of malaria infection. For example, bacterium-derived volatiles could be exploited to develop a new generation of mosquito repellents, or attractants for use as lures in traps for mosquito surveillance or control.

Skills and future career plans:

During my degree, I have developed several skills that I can use during the project, however, I am also keen to gain new skills and experiences during this PhD. I acquired some experience in microbiology, bioinformatics, molecular biology and next generation sequencing while undertaking a [removed] Microbiology studentship at [removed] working on the development of a molecular diagnostics approach to equine histoplasmosis. I thoroughly enjoyed the lab environment and the responsibility that came with having my own project. I am eager to build on those skills during the PhD project.

I have developed my knowledge of entomology through theory and practical modules based at the [HEI removed]. Additionally, I have collaborated with [removed] to learn the RNA interference (RNAi) technique which I needed for my honours project "RNAi of Mucin in determining disease severity". My honours project has given me the opportunity to apply the skills I have learnt over the last two years and my summer project. It has also given me the opportunity to work independently.

I have a major interest in infectious disease and disease control, gained through the opportunities I have taken to study and work in the lab at [removed]. I have some knowledge of designing and conducting experiments with mosquitoes from the vector biology module I did last year, but this PhD project would give me the opportunity to develop the practical components. I also have some experience of preparing DNA samples for high throughput sequencing and metagenomics analysis.

My aim is to become an independent researcher in academia in the future, working in the field of infectious disease, this project would give me the opportunity to develop the skills I need for this career path.

References:

Busula, A. O., N. O. Verhulst, T. Bousema, W. Takken, and J. G. de Boer. 2017. Mechanisms
of Plasmodium-Enhanced Attraction of Mosquito Vectors. Trends Parasitol. xx:1–13. Elsevier
Ltd.
Fernández-Grandon, G. M., S. A. Gezan, J. A. L. Armour, J. A. Pickett, and J. G. Logan. 2015.
Heritability of attractiveness to mosquitoes. PLoS One 10:1–10.
Logan, J. G., M. A. Birkett, S. J. Clark, S. Powers, N. J. Seal, L. J. Wadhams, A. J. Mordue, and
J. A. Pickett. 2008. Identification of human-derived volatile chemicals that interfere with attraction of Aedes aegypti mosquitoes. J. Chem. Ecol. 34:308–322.
Takken, W., and N. O. Verhulst. 2017. Chemical signaling in mosquito–host interactions: the role of human skin microbiota. Curr. Opin. Insect Sci. 20:68–74. Elsevier Inc.