

Project Details	
Project Code	MRC22IIARBa Nuetzmann
Title	The role of 'parasitism islands' in infection by soil-transmitted helminths
Research Theme	Infection, Immunity, Antimicrobial Resistance & Repair
Summary	Soil-transmitted helminths (STH) infect 1.5 billion people globally and cause a substantial global health burden. This project will investigate a novel concept in parasite biology: the physical organisation of important parasitism genes in genomic parasitism islands. In this project, we will investigate architecture, regulation and function of parasitism islands. Understanding the role of parasitism islands could lead to improved STH control and treatment strategies.
Description	Soil-transmitted helminths (STHs) infect 1.5 billion people globally and are estimated by the WHO to cause a disease burden greater than malaria or HIV/AIDS. Understanding the mechanisms parasites have evolved to infect their host is an important step towards developing much needed improvements in treatments and control methods. We have recently discovered that parasitism-associated genes in STHs e.g. genes coding for proteins that manipulate the host immune response, are physically clustered in the genome into 'parasitism islands'. These regions share many similarities with the pathogenicity islands that are well characterised in bacteria, and we hypothesise that parasitism islands have a fundamentally important role in parasite infection. Parasitism islands offer potential targets for anthelmintic drugs and alternative treatment strategies. This project will investigate the role and organisation of parasitism islands using a combination of lab-based and bioinformatic approaches, addressing questions such as: What is the functional role of parasitism islands in parasite-host interaction? How is gene expression regulated in parasitism islands? Are parasitism islands characteristic of parasite genomes in general? In the molecular biology component of the project, the student will work with the gastrointestinal parasitic nematode and STH, <i>Strongyloides ratti</i> , a well-established lab-model for parasite infection and a close relative of the human parasite <i>S. stercoralis</i> which infects 600 million people worldwide. The <i>Strongyloides</i> parasites are one of the few parasitic nematodes that CRISPR/Cas9 techniques have been established for and we use these methods to investigate the functional role of genes in parasitism islands. We will also perform functional analysis of epigenetic marks, including investigating the role of histone modifications and small RNAs in the regulation of virulence hotspots at different stages of infection. Based on our findings with the <i>S. ratti</i> the student will also carry out these methods on other helminth species, based in the Peachey lab. Together these approaches will help us to better understand the genetic toolbox used by parasites to successfully infect the host. Furthermore, identification of the key regulators of parasitism islands activity may lead to the development of advanced strategies to interfere with disease progression in infected patients. Throughout the project, the student will receive training in parasite culturing and biology, state-of-the-art molecular biology methods in transcriptomics, proteomics, histone biology, chromosome organisation and genetics. The student will also be trained in the bioinformatic analysis of large-scale genomic and transcriptomic datasets to investigate the role of

	<p>virulence hotspots in nematodes and parasites in general. The doctoral researcher will be integrated into ongoing collaborations with laboratories in Japan, Germany, UK and USA. For further background information about our research on gene organisation and parasites please visit <a href="https://researchportal.bath.ac.uk/en/persons/hans-wilhelm-nuetzmann">https://researchportal.bath.ac.uk/en/persons/hans-wilhelm-nuetzmann</a> <a href="http://www.vickyhuntlab.org">www.vickyhuntlab.org</a> <a href="http://www.bristol.ac.uk/vetscience/people/laura-e-peachey/overview.html">http://www.bristol.ac.uk/vetscience/people/laura-e-peachey/overview.html</a> and <a href="https://people.bath.ac.uk/bssldh/LaurenceDHurst/Home.html">https://people.bath.ac.uk/bssldh/LaurenceDHurst/Home.html</a></p>
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