

Project Details	
Project Code	MRCIAR24Ca Smith
Title	Once bitten, twice shy: the impact of helminth infection on viral immunity
Research Theme	Infection, Immunity, Antimicrobial Resistance & Repair
Summary	Although studies suggest that soil-transmitted helminth (STH)-infections influence human papillomavirus (HPV) infection (once bitten), it is not known how STH infection influence how they then deal with repeated exposure to the virus (twice shy). Using established in vitro assays, pre-clinical models and human samples, the aim of this project is to determine the processes by which STH influence immunity to pathogenic viral infections.
Description	<p>Approximately 1.45 billion people (&gt;20% of the world's population) are infected with one or more types of soil-transmitted helminth (STH). Within helminth-endemic areas, there are also very high levels of pathogenic viral infections, including human papillomavirus (HPV) infection. Although most HPV infections resolve, persistence of certain strains can result in warts, precancerous lesions and cervical cancer. Using viral particles, termed "pseudovirions", our lab has found that exposure to STH can significantly reduce HPV infection in vitro and in vivo [1,2]. However, epidemiological evidence has found that helminth exposed individuals have altered HPV strains, as well as an increased risk of HPV infection [3,4]. Interestingly, this increased risk of HPV infection is dependent on multiple partners and age, reflective of repeated exposure to HPV. Within STH endemic areas, the prevalence and death rate of HPV-related cervical cancer is higher than non-endemic areas [5]. It is therefore pertinent to understand how STH exposure influences viral immunity. We will determine the impact of STH on viral immunity in cell lines and mice through use of HPV pseudovirions in combination with the administration of the secretions of STH, or live infection with two well-characterised rodent models of human STH infection, <i>Nippostrongylus brasiliensis</i> and <i>Heligmosomoides polygyrus bakeri</i>. This information will be translated to human disease through analysis of biobanked samples from STH-endemic individuals exposed to pathological viral infections. Aim: This PhD will develop and test how STH infection influences viral immunity Objectives: 1) Using our established in vitro system, this project can determine how exposure to the secretions from rodent and human STH influence pseudovirion infection and challenge with the same or differing HPV serotypes. 2) Adapting our established pre-clinical rodent model, this project can determine how live infection with two well-characterised rodent models of human STH infection, <i>Nippostrongylus brasiliensis</i> and <i>Heligmosomoides polygyrus bakeri</i> impact on viral immunity in a well-characterised HPV vaccine (Gardasil)/HPV pseudovirion challenge model. 3) Using other pseudovirion constructs and a biobank of human serum and blood cell samples from patients living within STH endemic areas, this project could be extended to determine whether STH infection correlates with immunity to other important pathological viral infections, including the Dengue virus. The student will develop skills in literature review, experimental design, statistical analysis, data interpretation and critical analysis. They will also gain, at least, basic</p>

	<p>skills in tissue culture, pseudovirion production, virology, animal handling, parasitology, immunology and epidemiology. Depending on their interests, they may then develop specific areas of the proposed research aims. For example, they may focus on the results of in vitro experiments to investigate mechanisms by which STH infection impact on viral infection and challenge, or they may focus more on epidemiological data analysis of the cohort, extending knowledge of how STH infections impact on virus immunity in humans. Overall, the possibility to perform in vitro, pre-clinical and epidemiological analysis within a relevant co-infection field provides the successful candidate with the opportunity to receive multi-disciplinary training. The project is at the cutting edge of the field, studying an important clinically relevant issue that impacts on &gt;20% of the world's population. The training, knowledge and skills the PhD student develops during this project are translatable for a wide range of future career options. [1] <a href="https://doi.org/10.1038/s41598-018-30058-9">https://doi.org/10.1038/s41598-018-30058-9</a> [2] Butters C, Chetty A, Schafer G, Horsnell WCG, Smith KA., manuscript in preparation [3] <a href="https://doi.org/10.1093/infdis/jiy165">https://doi.org/10.1093/infdis/jiy165</a> [4] <a href="https://doi.org/10.3389/fmicb.2021.738894">https://doi.org/10.3389/fmicb.2021.738894</a> [5] Globocan 2020</p>
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