

Page 1 – General Information

Project Code	UGAB03
Partner University	University of Greenwich
Faculty/School/Department/Research Centres	Faculty of Engineering and Science, School of Science.
First supervisor Please provide name and weblink	Giulia Getti http://www.gre.ac.uk/engsci/study/lifesport/staff/giulia-getti
Second supervisor Please provide name and weblink	Joanna Miest
Third supervisor Please provide name and weblink	Susan Shorter
Fourth (external) supervisor	n/a
External/industrial supervisor	n/a
Which of the supervisors listed above is an early-career-researcher	Joanna Miest Susan Shorter
Contact details for project for informal applicant queries Email address	g.t.m.getti@gre.ac.uk
DTA Programme: Please delete as necessary which DTA programme this project relates to:	DTA Applied Biosciences for Health
Project title	Effect of aging on Leishmania infection: Ex vivo analysis of Leishmania infection of human blood.



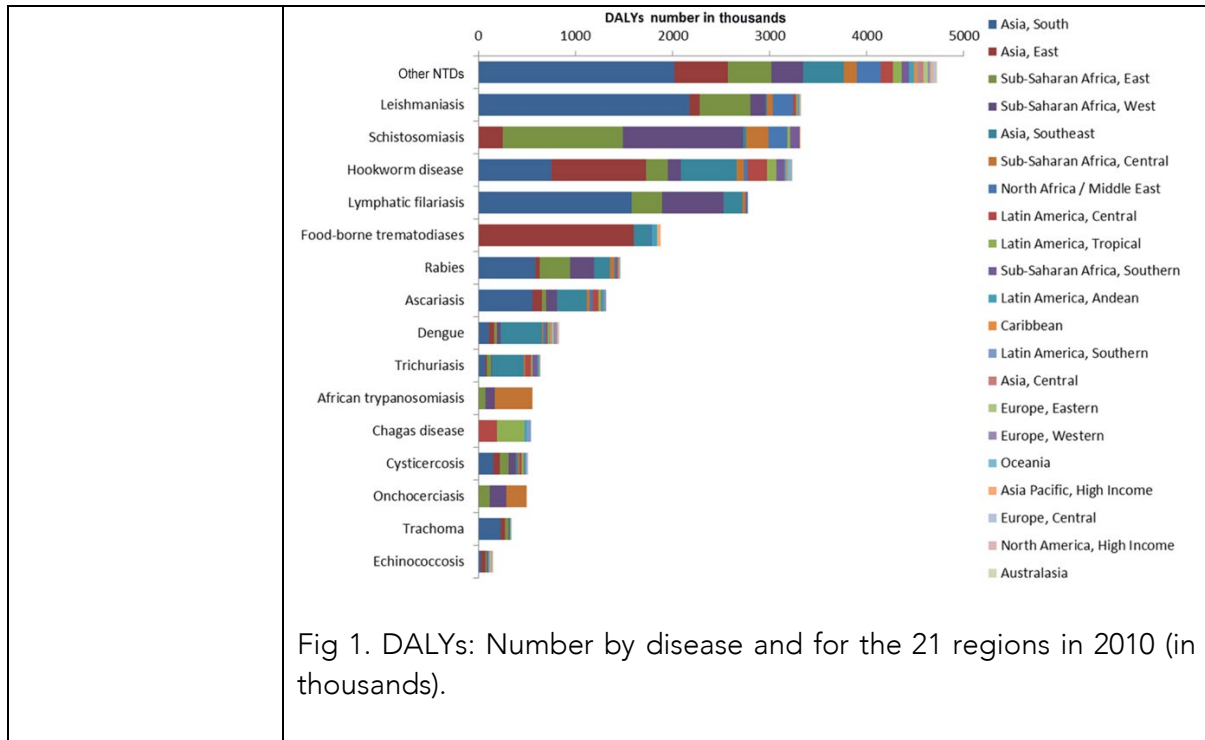
Page 2 – Project Description

Scientific Excellence (500 words)	<p>This research proposes to study how aging affects Leishmania spreading between human blood cells to tackle one of the least studied question of Leishmania research: changes in the immunology of infection during aging.</p> <p>Over 20 species of Leishmania are known to infect humans with consequent disease manifestation ranging from asymptomatic to self-healing cutaneous manifestation to deathly visceral infection. Disease outcome is a consequence of the immune response to infection. The effect of aging on immunological response and disease development has been investigated in mice models with contradictory results. Interestingly, asymptomatic infections are often detected in autopsy of elderly suggesting a link between an aging immune system and parasite survival within the host. A better understanding of the immunology of leishmaniasis is necessary to develop treatment and vaccination strategy. The immunology of Leishmania infection is a complex topic, which despite a significant amount of research remains largely misunderstood. This is largely due to the fact that almost all immunological studies are carried out on mice models which are not a good representation of infection and disease. Moreover almost all studies of infection investigate parasites entrance in human rather than their spreading between cells, even though disease manifestation is a direct consequence of the parasites ability to spread between host cells.</p>
Aim (400 words)	<p><u>Aim and hypothesis</u></p> <p>The aim of this research is to clarify the role of aging on parasites survival and spreading of Leishmania parasites on human peripheral blood derived immune cells.</p> <p>Our hypothesis is that the success of Leishmania spreading which is known to be linked to the host’s immunological response will change during aging in the human host.</p>



	<p><u>Methodology and Innovation</u></p> <p>The research will use peripheral blood derived monocytes and granulocytes (PBMCG) from human volunteers (divided into two groups, based on age) and genetically modified GFP-expressing parasites (1) to investigate infection. Percentage of infected cells from each population of cells will be detected via flow cytometry. Preliminary data from our laboratory (2) showed that Leishmania infection of sub-population of PBMCG varies over time suggesting that different cell types are involved at different stages of infection. The role of each cell subtypes will be investigated via a novel methodology developed in our lab to study infection spreading (3). The consequence of spreading on cytokine expression will be quantified via qPCR, and characteristics of the spreading mechanism will be detected via confocal and electron microscopy.</p>
<p>Strategic Relevance (300 words)</p>	<p><u>Strategic relevance</u></p> <p>This research will support the understanding and therefore the management of a disease, affecting the life of millions of people worldwide. Interestingly, unlike other widespread protozoan diseases leishmaniasis particularly affects the elderly as it is linked with increased mortality and morbidity in aging population. This is the opposite of what happens in similar infectious NTDs (Chagas disease and malaria). The rate of positive Leishmania skin test results among the elderly population in affected countries is high: 30%, 60%, and 70% in India, Brazil, and The Sudan, respectively. Thus, this infection is likely to become a relevant geriatric problem in affected countries. Leishmaniasis is responsible for the largest Neglected tropical diseases burden (Fig 1) and the ninth largest amongst all infectious diseases.</p>





<p>Interdisciplinarity and fit with DTA3</p>	<p>This research combines expertise Parasitology-Immunology (GG), Immunology-molecular biology (JM) and Cell biology-imaging (SS) to improving human health therefore is a perfect fit with the DTA program.</p>
<p>Industrial Relevance (300 words)</p>	<p>The project first supervisor has collaborations with various Universities including Imperial College, Wolverhampton University, The London School of Hygiene and tropical Medicine, East Anglia University, University of Portsmouth and Metropolitan University.</p>
<p>Economic and Societal Impact (300 words)</p>	<p>The improved understanding of disease manifestation and its link with aging and immune response will have a significant impact on the approaches used for managing and treating infection. Targeted therapies as well as novel approaches to vaccination will become possible. This will have a tremendous economic impact. As mentioned previously, Leishmaniasis is responsible for the largest NTDs burden on human population and the ninth largest amongst all infectious diseases. Neglected tropical diseases (NTDs) cost developing economies billions of dollars every year.</p>



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This project has received funding from the European Union’s Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 801604.

	<p>An even greater societal impact is expected. Leishmaniasis is a disfiguring and misunderstood disease. Stigmatization of individual affected by cutaneous infection occurs in all age groups: adolescents and children are isolated from their siblings by their parents and forbidden from attending school. Women are particularly victimized as they are no more considered suitable for marriage, sometimes by their own families. Mothers are often separated from their children and not allowed to breast-feed. Men are unable to find work and support their families. Unsurprisingly affected individuals suffer from depression and often anxiety with decrement in the quality of life and aging. As scars generally remain for years, the effect of infection affects individual for large parts of their lives. The impact of asymptomatic infection is also expected to increase with the growth of elderly populations, which are susceptible to developing severe symptoms as the immune system ability to limit parasites spread decreases. The increase in the lethality rates observed over the years in populations over 50 supports this expectation. This is of particular relevance in non-endemic countries, where diagnosis of leishmaniasis is likely to be delayed as infection is rare and linked to recent travel. An aging population on the other hand is likely to show symptoms years after contracting the infection and only as consequence of age-related reduction of immune defences. As the growth of the elderly population accelerates, leishmaniasis is expected to pose an increasing challenge to public health. By tackling the problem at early stages, its cost on the aging population in terms of mortality and morbidity can be greatly reduced.</p> <p>The scientific impact of studies on the immunology of Leishmania are not limited to improving the understanding of the disease itself but have allowed for our understanding of general human immunology to improve: Leishmania is the only parasite that has done for immunology more than immunology has done for Leishmania.</p>
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Page 3 – Admission Requirements

<p>Specific Admission Requirements Detail any subject specific degree qualifications or disciplines, relevant skills, experience</p>	<p>1st or Upper Second class degree (BSc) and/or postgraduate qualification in Biological Science or closely related subject.</p>
<p>Minimum IELTS score</p>	



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