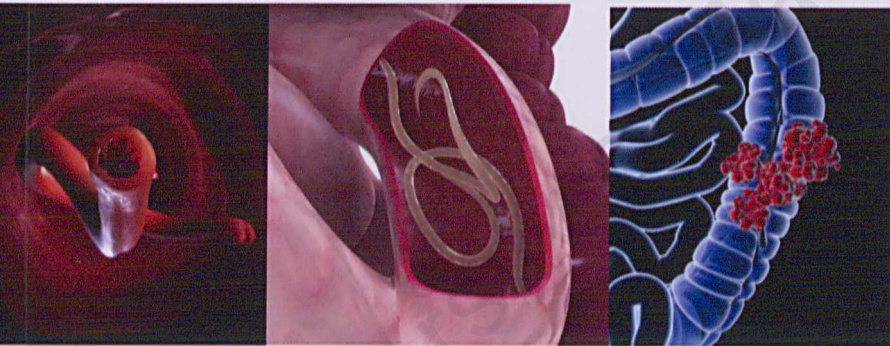


Debunking the myth about gut worms by unlocking the secrets of gut microbiota



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Inaugural Lecture & ASM Fellows' Lecture



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Malaysian Society of Parasitology
and Tropical Medicine

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SYNOPSIS

Debunking the myth about gut worms by unlocking the secrets of gut microbiota

Gut (Intestinal) worms have been described in ancient mummies dating from 1200 BC. In 2017, archaeological evidence of worms infecting ancient inhabitants of Greece was discovered in faeces collected from prehistoric burials confirming the writings of Hippocrates 2,500 years ago. These revelations provide concrete evidence that humans have co-evolved with worms for thousands of years, possibly since the emergence of our species. Gut worms such as *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm produce a wide range of symptoms including diarrhoea, abdominal pain, general malaise and weakness, whilst some cause intestinal blood loss. Chronic infections have been associated with impaired growth and cognitive development. In severe cases, these infections can cause gut obstruction, rectal prolapse and severe anaemia. Gut worms have always been associated with poor health, hence deworming programs are conducted worldwide to eradicate these worms from our human guts. However, in recent years, questions have been raised whether gut worms are really such nasty creatures after all. There is even a growing interest that gut worms may play a role in the future treatment of inflammatory diseases. How did this come about? Let me take you on my journey of discovery to unlock the secrets of gut worms and gut microbiota.

BIODATA

PROFESSOR DR YVONNE LIM AI LIAN

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Professor Dr Yvonne Lim Ai Lian joined the Department of Parasitology, Faculty of Medicine, University of Malaya, Kuala Lumpur in November 2003. Her early education began at the Infant Jesus Convent, Malacca, followed by the Malacca High School. She then obtained her BSc and PhD from Universiti Kebangsaan Malaysia (UKM). After graduating, she taught at the Faculty of Science and Technology, Universiti Kebangsaan Malaysia (UKM) and Tunku Abdul Rahman College (now Tunku Abdul Rahman University College) before joining University of Malaya (UM). She also had the privilege of training under the tutelage of the late Professor Dr Huw Vaughan Smith (consultant clinical parasitologist and director of the Scottish Parasite Diagnostic Laboratory in Glasgow, Scotland) and Professor Dr Robin B. Gasser (University of Melbourne, Australia).

Currently, she is the Deputy Dean (Research) of the Faculty of Medicine, University of Malaya. She is also the environmental section head of Parasites: South East Asian Diagnostic Laboratory (Para:SEAD) at the Department of Parasitology, Faculty of Medicine, University of Malaya. Previously, she was the faculty coordinator of stage two MBBS programme and head coordinator of the postgraduate programme.

Professor Lim is a versatile and committed academician who loves teaching and enjoys research. She has been teaching Parasitology to the medical, pharmacy, biomedical, nursing and medical laboratory technology students for the past 15 years. Recently in 2018, she and her co-authors wrote a textbook on "Medical Parasitology: A textbook" which was published by Springer.

Her research focuses on neglected tropical diseases primarily among marginalised populations (e.g., Orang Asli communities, migrant workers) using tools such as Geographic Information System (GIS) and next generation sequencing (NGS) to map and understand these diseases among these

populations. More recently, she began exploring the molecular mechanisms that underpin the interactions between parasitic infections, in particular gut worm infections, nutritional status, gut microbiota (bacteria) and the inflammatory responses. Her research has been funded by internal university grants and external grants from the Ministry of Science, Technology and Innovation (MOSTI), Ministry of Higher Education (MOHE) and Ministry of Health (MOH). This year, together with her collaborator at the New York University, they succeeded in securing a highly competitive US National Institutes of Health (NIH) grant for a period of 5 years (2018-2022).

Over the years, she has supervised to completion a total of 10 PhD and 12 MSc students. She encourages her postgraduate students to be attached and trained in various illustrious institutions, believing that her students will benefit tremendously from international exposure. Some of these institutions include the London School of Hygiene & Tropical Medicine, United Kingdom; New York University, United States (via the Merdeka Award Grant for International Attachment); University of Melbourne, Australia (via the Australian Endeavour Research Fellowship), Academia Sinica, Taiwan and Institut Pasteur of Shanghai, China (sponsored by Institut Pasteur of Shanghai-Chinese Academy of Sciences (IPS-CAS)). These mobility activities have been instrumental in maintaining and strengthening partnerships between UM and these august institutions. In return, Professor Lim has also hosted many students from countries such as Singapore, Indonesia, Philippines, Australia and the United States for various research stints.

Through her network, UM has been the beneficiary of such strong ties with several international and regional institutions. Similarly, at the local arena, she works with various public and private agencies, namely Ministry of Health, Ministry of Agriculture and Agro-Based Industry Malaysia, Department of Orang Asli Development (JAKOA), Hospital Orang Asli Gombak, Veterinary Research Institute (VRI) and various local public and private universities. Her expertise and reputation in the field of Parasitology are recognised by the many invitations to present at international and national conferences as well as invites to be external examiner of PhD theses from national and international universities (e.g., Australia, Denmark).

Since she joined UM in November 2003, she has authored more than 150 original papers, written seven book chapters, edited and written three books, in particular "Parasites and their vectors: A special focus on Southeast Asia" (Springer, 2013) and "Medical Parasitology: A textbook" (Springer, 2018). Her work is well cited with a total of 1204 citations and a H-index of 20.

Her latest landmark publication with collaborators from New York University (NYU) Langone Medical Centre and other institutions in the prestigious journal

of SCIENCE April 2016 (impact Factor 37.205) described the discovery of the mechanisms of how low levels of worm infection promote growth of probiotic bacteria that might in future assist treatment of inflammatory bowel diseases (IBD) such as Crohn's Disease and ulcerative colitis.

Professor Lim is a strong believer in team effort and has over the years developed a firm ASEAN network and is a regional speaker in her area of expertise. She has been an active member of the Malaysian Society of Parasitology and Tropical Medicine (MSPTM) since 1996. She has served as council member, treasurer, secretary, vice president and president (2014-2015) of the Society. She was one of the assistant editors of an ISI journal, Tropical Biomedicine from 2010-2014. In 2008, she was the recipient of the 2007 Malaysian Society of Parasitology and Tropical Medicine (MSPTM) Medal which is awarded to young researchers for outstanding research in the field of Parasitology and Tropical Medicine. That same year, she was awarded the Royal Society of Tropical Medicine and Hygiene Centenary Scholarship (London).

In 2015, UM recognized her efforts and awarded her the Excellent Lecturer (Science), UM Excellence Awards 2015. The year after, in 2016, she received the Top Research Scientists Malaysia (TRSM) 2016 award and in 2017, she was inducted as a fellow of the Academy of Sciences Malaysia.

DEBUNKING THE MYTH ABOUT GUT WORMS BY UNLOCKING THE SECRETS OF GUT MICROBIOTA

Introduction

In 2017, University of Cambridge researchers together with Greek archaeologists discovered faecal evidence of worms collected from prehistoric burials infecting ancient inhabitants of Island of Kea, Greece (Anastasiou et al., 2017). This discovery confirmed what Hippocrates had written 2,500 years ago and proved that humans have co-existed with worms over thousands of years. Parasitic worms such as *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm live within the human gut, obtaining nourishment and protection while seemingly offering no benefit in return to humans. Gut worms can produce a wide range of symptoms including intestinal manifestations (diarrhoea, abdominal pain), general malaise and weakness. Chronic infections have also been associated with impaired growth and cognitive development resulting in poor academic performance. In severe cases, these infections may cause gut obstruction, rectal prolapse and severe anaemia.

Today, more than 24% of the world's population is afflicted with at least one of these gut worms (Pullan et al., 2014; Ngui et al., 2015; Tunbosun et al., 2017; WHO, 2017). In the Southeast Asian region, each worm infection is associated with approximately 100 million infections (Pullan et al., 2014; Ngui et al., 2012a, b). In Malaysia, gut worm infections are largely controlled (Anon., 2008a) due to the Malaysian government's effort in employing a variety of strategies, including the use of deworming regimens in schools, clinics or mobile facilities in rural and indigenous areas as well as educational awareness campaigns (Anon., 2008b). However, foci of high endemicity (with prevalences of 5.5–98.2% for *Trichuris*, 8.0–67.8% for *Ascaris*, and 3.0–44.7% for hookworms) still persist in some rural areas and within certain indigenous and tribal communities (Zulkifli et al., 2000; Al-Mekhlafi et al., 2008) in which sanitation is often poor.

Efforts to combat worm infections

a) Re-initiating deworming programme

Malaysia's nationwide deworming programme was discontinued in 1983 given the overall decline in the prevalence of worm infections. Nonetheless, in certain disadvantaged communities, these infections have persisted. In 2007, our team obtained an E-Science grant from the Ministry of Science, Technology and Innovation (MOSTI) to conduct a comprehensive study on the status of worm infections among indigenous communities residing in Peninsular

Malaysia. A total of 716 participants from 9 Orang Asli villages participated, comprising those aged from 1 to 83 years old. The overall prevalence of the worm infection was 73.2% (Ngui et al. 2011a). This study represented the largest study since 1991 and the results of the study was presented to the Director of the Department of Orang Asli Development (JAKOA) in 2010. Based on the evidence and following the outcome of the National Action Council (MKN) in that same year, deworming programmes were re-initiated. According to JAKOA's Annual Report 2011 (page 74), the deworming activities were performed from house to house to identify the Orang Asli children and adult in need of treatment. Liquid albendazole was given to children aged 2-12 years old whilst albendazole tablet (400 mg) was given to those more than 12 years old. A total of 1605 Orang Asli benefited from this treatment programme.

b) Providing enhanced and pragmatic solutions for worm infections via the utilisation of advanced technology

One of the major challenges of treatment is that the prevalence of worm reinfections can return to near pre-treatment levels in just 6 months following deworming (Al-Mekhlafi et al., 2008). Multipronged control measures are needed which include routine treatment and health education. Our team developed a school-based programme called HELP (Health Educational Learning Package) in which teachers and Orang Asli school children are empowered with the knowledge on worm infections and ways to curb the infections. This was done with the provision of HELP packages whereby each participating child was given a comic book, posters with health messages, a pair of slippers (to prevent hookworm infection), a nail clipper and soap. Health messages were also taught through songs, colouring activities, competitions and puppet shows. In addition, deworming drugs were also administered to infected children. The package was well-received with effective contributions being made by teachers, children and their parents. The incidence rates of worm infection at different assessment points declined significantly among children receiving both the deworming drugs and health education compared to those in the control school (received only deworming drugs). Similarly, the intensity of trichuriasis, ascariasis and hookworm infections were found to be significantly lower among children receiving both the deworming drugs and health education compared to those in the control group ($p < 0.05$) (Al-Delaimy et al., 2014).

In resource limited settings especially in the Orang Asli communities, it is crucial that treatment and health education are delivered to the most needed communities and to the targeted localities. To fill this gap, our team developed predictive maps of worm infections using the advanced Geographic Information System (GIS) tools. GIS not only allows us to map and visualise the locations of populations with high prevalence rates but importantly to estimate the number of individuals to treat with deworming drugs in these populations.

These estimates enable evidence-based decision making and save cost. We managed to assemble a database from 99 different locations and this effort represented one of the most comprehensive compilations of worm infections in the country. The GIS analysis resulted in a predictive map and crucial information on estimated numbers of individuals to treat for all 78 districts in the whole of Peninsular Malaysia (Ngui et al., 2014). These data have been submitted to the Indigenous Health Unit, Ministry of Health to assist in effective implementation of sustainable worm infection control programmes.

Sighting of an intriguing observation – inverse association between gut worms and asthma

Two features that were frequently observed in many outcomes of our epidemiological studies were that most of those infected with worms were asymptomatic (no symptoms) and that the infections were chronic. In addition, an intriguing finding which led us into a new research pathway was the evidence of low prevalence of confirmed bronchial asthma (i.e., 1.4% of 716) observed in communities with high prevalence of worm infections (i.e., 73.2% of 716) (Ngui et al. 2011a, b). Our team found that asthma was not common in rural subsistence communities. This inverse relationship was in concordance with findings of a large epidemiological study in Ethiopia by Scrivener et al. (2001) who observed that the risk of asthma is reduced by the presence of gut worms.

Gut worms usually remain in human gut for years obtaining nourishment and protection whilst humans presume that these organisms do not offer any benefit in return. To ensure their long-term survival, worms have evolved amazing strategies to either avoid or regulate the host immune responses. The maintenance of the asymptomatic state is now recognized as reflecting an immunoregulatory environment, which may be promoted by the worms.

The wormy war: Foes or friends?

The above-mentioned behavior of the worms reflects aptly a quote from the famous Chinese philosopher, Sun Tzu. He once said in his book *“The Art of War”* - *Be so subtle that you are invisible, be so mysterious that you are intangible and then you will control your rival's fate.* Worms are indeed war strategists for they know that for their own survival, they need to be subtle.

Debunking the myth about gut worms by unlocking the secrets of gut microbiota

In recent years, there is increasing interest in whether worm-associated immune regulation may ameliorate allergy and autoimmunity. It was hypothesised that understanding and exploiting the interactions between these worms and the host regulatory network may highlight new strategies to control both infectious and immunological diseases (McSorley and Maizels, 2012). Worms do that by influencing the co-inhabitants of the gut (e.g., bacteria, viruses, fungi, protozoa) through mutualistic and synergistic interactions (Png and Lim, 2016).

Given the lack of information on how the presence of worms influence the gut microbiota (bacteria) in human studies, our team embarked on a project in 2012 to compare the gut microbiota of worm infected individuals with individuals who were not infected with worms. We undertook this adventure with our collaborator, Associate Professor Dr Png Loke from New York University (NYU). We compared the composition and diversity of bacterial communities using next generation sequencing (NGS) analysis from the faecal microbiota of 51 people from two villages in Malaysia, of which 36 (70.6%) were infected by worms.

As observed in **Fig. 1**, worm infected individuals especially with the worm *Trichuris* had an increase in gut bacterial species diversity. This has great significance as higher microbiota diversity (as seen in infected worm individuals), has generally been associated with better health. This finding highlighted that low burden of worm infections may have a positive impact on the diversity, bacterial community structure and function of the gut microbiome (Lee et al., 2014). We hypothesised that these relationships could be exploited therapeutically for future treatment of inflammatory diseases such as inflammatory bowel disease (IBD).

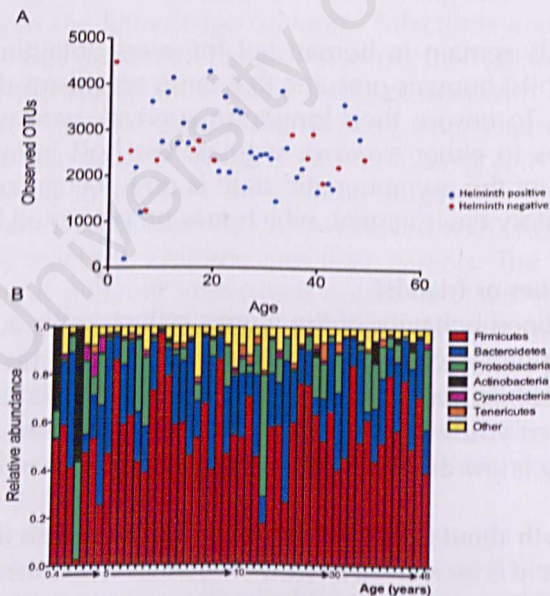


Figure 1. Abundance and diversity in the intestinal microbiome in 51 Malaysian subjects. (Panel A) The number of observed OTUs plotted against age for all 51 individual samples. The number of observed OTUs for most samples was between 1500–4000. (Panel B) Relative abundance of the top phyla represented across the 51 subjects arranged by increasing age. The abundance patterns were largely similar across the individual subjects, except in two of the younger subjects who had high abundance of Actinobacteria (*Bifidobacterium* sp.) in their stool samples.

Can worms be used to treat inflammatory bowel disease (IBD)?

In 2016, our team discovered a possible pathway that potentially allows gut worms to help treat inflammatory bowel diseases (IBD) such as Crohn's Disease and ulcerative colitis. In our work published in **SCIENCE** (Ramanan et al., 2016), we found that infection with gut worms in mice model of Crohn's disease increased the number of *Clostridia* bacterial species, which are known to be "anti-inflammatory", and decreased the abundance of *Bacteroides*, bacteria which is thought to promote IBD, as much as a thousand-fold.

A member of our team developed a mouse model of Crohn's disease (Ramanan et al, 2014) based on the understanding that polymorphisms in human *Nod2* are associated with inflammatory bowel diseases (Cleyne et al, 2016). We found that mice deficient in *Nod2* develop intestinal abnormalities. The most notable abnormality in these mice was goblet cells (secrete mucus) defect that resulted in a compromised mucus layer, allowing sustained colonisation by *Bacteroides vulgatus* (Ramanan et al, 2014).

Using this mouse model, we infected the *Nod2* deficient mice with the gut worm *Trichuris muris*. We noted that following the worm infection, goblet cell defects were completely restored (Fig. 2a). Inflammatory markers (Reg3 β and IFN- γ +CD8+IELs) were also reduced (Fig. 2b). As the mucus layer improves via the type 2 immune response (i.e., IL-13 or IL-4), *Clostridia* strains expand due to conducive environment and thus outcompete the *Bacteroides* either for resources needed for survival or by releasing toxins harmful for *Bacteroides*.

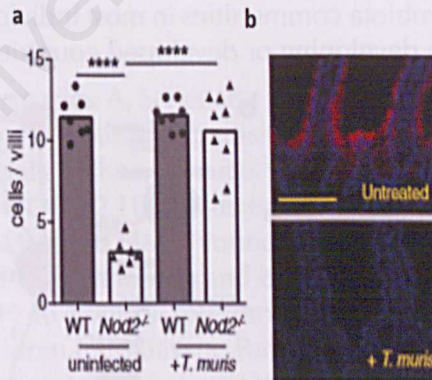


Figure 2. *T. muris* infection of *Nod2* deficient mice (a) restores goblet cell defects, (b) reduces inflammatory markers e.g. Reg3 β

In addition to the mouse model, our team simultaneously conducted human field cross-sectional study and found that *Trichuris* infected individuals in rural Malaysia have higher microbial diversity than *Trichuris* negative individuals

(Lee et al, 2014). We then conducted a pilot longitudinal treatment study, whereby we analysed stool samples collected from 75 infected individuals before and after deworming treatment with albendazole. Consistent with our cross-sectional study, diversity of microbial communities was significantly reduced after deworming (**Fig. 3a**) and Clostridiales was the most significantly reduced order, whereas Bacteroidales (Prevotella) was significantly expanded after treatment (**Fig. 3b**) (Ramanan et al, 2016).

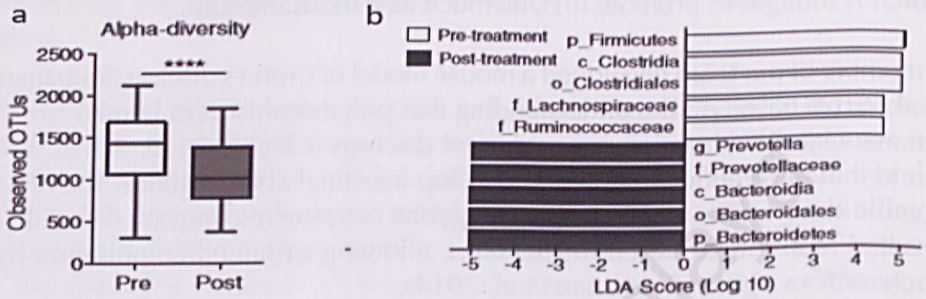


Figure 3. Microbiota of the Orang Asli (a) Microbial diversity is reduced after deworming (b) Clostridiales are reduced and Bacteroidales are increased after deworming.

With these datasets, our team then developed a novel strategy to characterize the microbiota dataset using the egg-burden information. We combined centered log-ratio (clr) transformation with partial least squares (PLS) regression to examine within-subject changes, incorporating a repeated measures design. We found that the antagonistic relationship we discovered between Clostridiales and Bacteroidales that is promoted by worm infection may actually be a general principle for the gut microbiota communities in most individuals, regardless of their living conditions in developing or developed countries (**Fig. 4**).

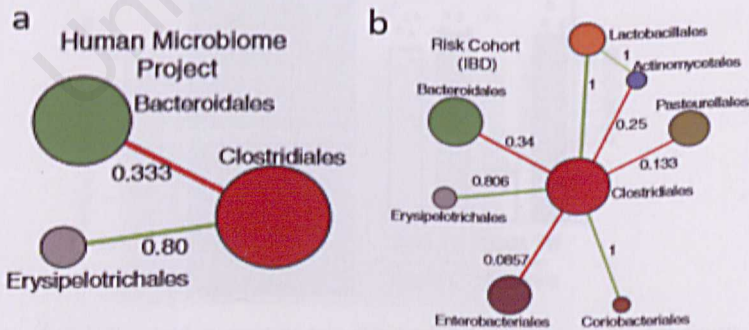


Figure 4. Helminth colonization in humans is associated with a decrease in Bacteroidales and an increase in Clostridiales levels. (a and b) Microbial network inference demonstrating an antagonistic relationship between Clostridiales and Bacteroidales communities from the Human Microbiome Project (a) and the pediatric IBD RISKcohort (b).

These findings were among the first to uncover the mechanisms by which worms could be potentially used as therapeutic agents for IBD. This collaborative study was a significant outcome of an on-going collaboration between University of Malaya and New York University which was partly funded by the University of Malaya-Ministry of Higher Education High Impact Research (UM MOHE-HIR) grant. Other funds that supported this study included the National Institute of Health (USA) and the Burroughs Wellcome Fund. In addition, we also collaborated with Center for Integrative Medical Sciences in Yokohama, Japan and the Center for Immunity and Inflammation at New Jersey Medical School.

Our discovery continues... What's next?

In our on-going study, we will be assessing the effects of deworming drug treatment on the gut microbiota in humans by metagenomics analysis. Along with dietary surveys, the proposed field studies will provide longitudinal analyses of worm infected individuals to establish cause and effect relationships of gut worms on the gut microbiota composition and function. We also intend to explore the use of worm infections as a treatment agent for other inflammatory diseases as well.

These on-going projects are now funded by the United States National Institutes of Health (NIH) for 5 years (2018-2022). This is an exciting opportunity to build on the momentum and to add to our current knowledge. We hope to both find strategies to improve deworming efficacy in communities that require deworming and to develop new therapeutic strategies for manipulating the microbiota in individuals suffering from inflammatory diseases caused by microbial dysbiosis.

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PRESENT APPOINTMENT

Deputy Dean (Research), Faculty of Medicine, University of Malaya

ACADEMIC QUALIFICATION

PhD, BSc (UKM)

SELECTED PUBLICATIONS

Books

1. Rohela Mahmud, **Yvonne AL Lim**, Amirah Amir. Medical Parasitology: A Textbook. Springer 2018.
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SELECTED RESEARCH PROJECTS

National and International Grants

| No | Title | Source | Start | End | Role |
|----|--|--|-------|------|-----------------------------|
| 1. | Incorporating vision-based technique for <i>Cryptosporidium</i> and <i>Giardia</i> detection in water and food industry | ERGS MOHE | 2011 | 2013 | Co-Investigator |
| 2. | Malaysian medicinal plants: A search for macrofilaricidal activity towards improving the current control strategies for the elimination of lymphatic filariasis. | FRGS MOHE | 2011 | 2013 | Co-Investigator |
| 3. | High-resolution melting approach for rapid and effective evaluation of helminth in mixed-helminthes population samples. | EScience MOSTI | 2012 | 2014 | Principal Investigator (PI) |
| 4. | Effects of nutritional status and helminth infections on gut bacteria and inflammatory responses in Malaysian populations | UM-MOHE High Impact Research (HIR) Grant | 2013 | 2015 | Principal Investigator |
| 5. | Protective immune responses to the blood stages of infection of long tailed macaques by <i>Plasmodium knowlesi</i> | ERGS MOHE | 2013 | 2015 | Co-Investigator |
| 6. | Molecular phylogenies of <i>Blastocystis</i> sp. isolates from different hosts: Identification of subtypes, implication for pathogenicity and zoonosis | RAGS | 2014 | 2016 | Co-Investigator |

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|-----|--|--------------|------|------|---------------------------|
| 7. | Parasitic and microbial infections amongst urban poor communities in Malaysia | FRGS MOHE | 2014 | 2017 | Co-Investigator |
| 8. | The mechanism of interactions between STH and gut microbiota by molecular analysis in Malaysia: A supplementary model to hygiene hypothesis | FRGS MOHE | 2015 | 2016 | Co-Investigator |
| 9. | Molecular characterisation of apical membrane antigen 1 of <i>Plasmodium knowlesi</i> (PkAMA1) | FRGS MOHE | 2015 | 2016 | Co-Investigator |
| 10. | Identification of novel antimalarial agents for the treatment of <i>knowlesi</i> malaria via in silico screening and enzymatic inhibition analysis | RAGS | 2015 | 2016 | Co-Investigator |
| 11. | Modulation of human immune responses by cohabitation of intestinal helminths and gut bacteria | FRGS MOHE | 2017 | 2020 | Principle Investigator |
| 12. | Interactions between helminth colonisation and the gut microbiota | US NIH Grant | 2018 | 2022 | Co-Principle Investigator |

Internal Grant

| No | Title | Amount of Financial Assistance | Start | End | Role |
|----|---|------------------------------------|-------|------|------------------------|
| 1. | The environmental and human behavior influences on <i>Aedes</i> intensity | UMRG | 2011 | 2013 | Co-Investigator |
| 2. | Genotyping and subgenotyping of <i>Giardia</i> and <i>Cryptosporidium</i> among indigenous people in Malaysia | UMRG | 2011 | 2014 | Principal Investigator |
| 3. | Genetic diversity and population structure of <i>Plasmodium</i> isolates obtained from confirmed cases of malaria | UMRG | 2012 | 2013 | Co-Investigator |
| 4. | Detection of waterborne in water treatment plants in Sarawak, Malaysia | PPP | 2012 | 2013 | Principal Investigator |
| 5. | The phylogeography and ecology of human and non-human primate malarias and their vectors in Malaysia | UMRG | 2012 | 2014 | Co-Investigator |
| 6. | Investigation of the gut microbiota in healthy Malaysian population | UMRG | 2013 | 2014 | Co-Investigator |
| 7. | Health Education Learning Package (HELP) to control intestinal parasitic infections among the Orang Asli populations in rural Peninsular Malaysia | Flagship - SBS (Equitable Society) | 2013 | 2014 | Principle Investigator |

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|-----|---|------|------|------|------------------------|
| 8. | Innate immune response against <i>Plasmodium falciparum</i> and <i>P. knowlesi</i> among Malaysian healthy individuals | UMRG | 2013 | 2014 | Co-Investigator |
| 9. | Molecular identification and characterisation of human malaria parasites and <i>In vitro</i> studies of SICAvr gene transcription of <i>Plasmodium knowlesi</i> -infected erythrocytes induced by adhesion of different host cell receptors | PPP | 2013 | 2015 | Principal Investigator |
| 10. | Association among parasitic infections, nutritional status, socioeconomic and environmental sanitary behavior among communities in Sarikei and Kapit Divisions, Sarawak | UMRG | 2014 | 2015 | Co-Investigator |
| 11. | Isolation and characterisation of parasites from various water types in Malaysia | UMRG | 2014 | 2015 | Co-Investigator |
| 12. | Synergistic effects of helminth and gut microbiota in human host immune system | BKP | 2017 | 2018 | Principle investigator |
| 13. | Molecular characterisation of <i>Dirofilaria</i> parasites and their association with vectors and canine | PPP | 2016 | 2019 | Principle investigator |

Consultancies (Registered with UPUM)

| No | Activity | Organisation | Role | Start | End | Level |
|----|--|--|------------|-------|------|----------|
| 1. | Consultancy services and laboratory analysis of waterborne parasites | Gamuda Water Sdn | Consultant | 2011 | 2016 | National |
| 2. | Consultancy services and laboratory analysis of waterborne parasites | Lembaga Air Kuching | Consultant | 2012 | 2012 | National |
| 3. | Consultancy services and laboratory analysis of waterborne parasites | Taliworks Sdn Bhd | Consultant | 2013 | 2017 | National |
| 4. | Kajian penyaringan kehadiran <i>Cryptosporidium</i> sp. dalam sampel air loji rawatan air terpilih | Division of Engineering Services, Ministry of Health | Consultant | 2015 | 2015 | National |
| 5. | Consultancy services and laboratory analysis of waterborne parasites | ALS Technichem Sdn Bhd | Consultant | 2017 | 2018 | National |

POSTGRADUATE SUPERVISION

PhD

| No | Name of postgraduate | Title of research |
|-----|--|--|
| 1. | Muhammed Abdu Khalid Mahdy (MHA050004) (International) | Molecular identification and genotyping of intestinal protozoa isolated from human, animal and environmental samples |
| 2. | Asma Iqbal (MHA080002) (International) | Genotyping of <i>Cryptosporidium</i> in immunocompromised patients |
| 3. | Naelah Abdulaziz Abdel Wale Mahuob Alyousefi (MHA080040) (International) | Molecular epidemiology of <i>Cryptosporidium</i> and <i>Giardia duodenalis</i> in Sana'a City, Yemen |
| 4. | Romano Ngui (MHA100031) | Development of novel diagnostic technique and geospatial database for soil-transmitted helminthiasis in Malaysia |
| 5. | Chew Ching Hoong (MHA080016) | Development of malaria detection systems through genomic and proteomic approaches |
| 6. | Ahmad Khalaf Soofi Al-Delaimy (MHA100036) (International) | The impact of Health Education Learning Package (HELP) in controlling soil-transmitted helminthiasis in Orang Asli communities |
| 7. | Lee Soo Ching (MHA120041) | Effects of intestinal helminth colonisation on gut microbiota diversity and composition |
| 8. | Tan Tiong Kai (MHA120040) | Genotyping of <i>Haemonchus contortus</i> among livestock in Malaysia and characterisation of benzimidazole resistance profile through genomic and proteomic approaches |
| 9. | Omar Bamaga (MHA100059) (International) | Molecular epidemiology of malaria and detection of antimalarial drug resistance-associated markers (<i>Pfcr</i> , <i>Pfmdr-1</i> , <i>Pfdhfr</i> And <i>Pfdhps</i>) in Hadhramout Governorate, Yemen |
| 10. | Norhidayu binti Sahimin (SHC130051) | Parasitic infections amongst migrant workers in Malaysia |
| 11. | Goh Xiang Ting (MHA140030) | Genotyping of human malaria parasites and the identification of binding peptides targeting PkMSP-1 ₁₉ |

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| 12. | Yap Nan Jiun (MHA120062) | Molecular characterisation of human and simian <i>Plasmodium</i> species among indigenous people in Malaysia |
| 13. | Chua Ling Ling (MHA150057) | Association between gut microbiome dysbiosis with systemic immune activation, inflammation and early onset of age-related comorbidities |
| 14. | Norashikin @ Suzani bt Mohd Shaharuddin (MHA140038) | Genetic characterisation and virulence genes profiling of soil-transmitted helminths in Malaysia |
| 15. | Donea Abdulrazak Abdullah (Registered with UPM, Malaysia) | Molecular epidemiology, genetic characterisation and phylogenetics of zoonotic enteric and tissue protozoa of livestock in Malaysia |
| 16. | Vinnie Siow Wei Yin (MHA150047) | Molecular characterisation of <i>Dirofilaria</i> parasites and their association with vectors and canine |
| 17. | Tee Mian Zi (MHA150046) | Gut microbiome, metabolome and molecular characterisation of iron metabolism genes in patients with thalassemia |
| 18. | Azdayanti Muslim (MHA160007) | The effects of intestinal parasitic infections on the composition of gut microbiota and metabolomics profiles before and after albendazole administration among Negrito Orang Asli |
| 19. | Lai Jing Wei (SHC160050) | Development of copper(II) and zinc(II) complexes against pathogenic protozoa via multiple targeting |
| 20. | Pavitra a/p Soosai Peranathan (MVA170003) | Host preferences of blackflies and their associated filarial parasites in Malaysia |
| 21. | Nabil Ahmed Mohammed Nasr (MHA130080) (International) | Promoting Health Education Learning Package (HELP) against intestinal parasitic infections among Orang Asli communities in Malaysia |
| 22. | Wan Najdah Wan Mohamad Ali (MHA150016) | Distribution maps of denv-infected <i>Aedes</i> mosquitoes, their resistance and enzymatic levels from <i>Aedes</i> mosquitoes collected from dengue hotspot areas in Kuala Lumpur and Selangor |

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| 23. | Reena Leeba Anak Richard (SVA170034) | Water for socially inclusive development in rural Malaysia |
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MSc

| No | Name of postgraduate | Title of research |
|-----|--|---|
| 1. | Harimah bte Hamdan (Registered with UTM, Malaysia) | Detection of <i>Cryptosporidium</i> and <i>Giardia</i> in drinking water |
| 2. | Romano Ngui . (MGN080015) | Soil-transmitted helminthes infection and asthma among the Orang Asli in Malaysia |
| 3. | Albana Sejдини (MGN080017) (International) | Giardiasis among pre-school children of low socio-economic background in the district of Elbasan, Albania |
| 4. | Lo Nyuk Ting (Registered with Nagoya University, Japan) | <i>Cryptosporidium</i> and <i>Giardia</i> in drinking water |
| 5. | Thulasi A/P Kumar (MGN110016) | Isolation and characterisation of waterborne pathogenic parasites in Malaysia |
| 6. | Subashini A/P Onichandran (MGN130027) | Waterborne parasites and its association with physicochemical parameters in Malaysia and the Philippines |
| 7. | Lorraine Angal (MGN120010) | Current status of intestinal parasitic infections among immunocompetent and immunocompromised prison inmates |
| 8. | Reena Leeba Anak Richard (MGN120011) | Detection of waterborne pathogens in water treatment plants in Sarawak, Malaysia. |
| 9. | Yamuna A/P Rajoo (Registered with International Medical University [IMU]) | Association between intestinal parasitic infections, nutritional status, socioeconomic and environmental sanitary behavior among long houses communities in Sarikei Division, Sarawak |
| 10. | Chin Yuee Teng (MGN140033) | Assessment of gut microbiome to parasitic infections among indigenous communities in Malaysia |

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| 11. | Noor Afizah Ahmad (MGN130014) | Detection of <i>Wolbachia</i> in <i>Aedes albopictus</i> from mainland and islands and their effects on chikungunya virus |
| 12.. | Hafizatul Anis binti Mohamed Zan (MGN130015) | Scrub typhus: disease prevalence, identification of potential vectors and use of molecular method for detection of <i>Orientia tsutsugamushi</i> |
| 13. | Habibi binti Hassan (MGN120027) | Prevalence of dengue in rural and forest periphery areas at Malaysia |
| 14. | Nur Amirah binti Hassan (MGN160016) | Molecular characterisation and associated clinical manifestation of enteric opportunistic parasites among immunocompromised patients |

SELECTED APPOINTMENTS / EXPERT PANEL

International

| No | Role |
|----|--|
| 1. | Organizing Committee of the 6 th ASEAN Congress of Tropical Medicine and Parasitology and 50 th Malaysian Society of Parasitology and Tropical Medicine. 5-7 March 2014 Intercontinental Kuala Lumpur, Malaysia |
| 2. | Chairperson of the Keynote Address by Robin Gasser, Australia, 6 March 2014 – Tackling neglected tropical disease pathogens using next-generation technologies: prospects and need for public-private partnerships) for 6 th ASEAN Congress of Tropical Medicine and Parasitology and 50 th Malaysian Society of Parasitology and Tropical Medicine. 5-7 March 2014, Intercontinental Kuala Lumpur, Malaysia |
| 3. | Steering Committee. 7 th ASEAN Congress of Tropical Medicine and Parasitology and 3 rd International Conference on Molecular and Clinical Aspects of HIV-AIDS, Tuberculosis and Malaria. 17-19 May 2016, Savana Hotel and Convention, Malang, Indonesia |
| 4. | Moderator. 7 th ASEAN Congress of Tropical Medicine and Parasitology and 3 rd International Conference on Molecular and Clinical Aspects of HIV-AIDS, Tuberculosis and Malaria. 17-19 May 2016, Savana Hotel and Convention, Malang, Indonesia |
| 5. | Local Organising Committee for the 26 th International Conference of the World Association for the Advancement of Veterinary Parasitology (WAAVP). 4-8 September, 2017, Kuala Lumpur Convention Centre, Malaysia |

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| 6. | Co-chair of Scientific and Research Subcommittee for the 26 th International Conference of the World Association for the Advancement of Veterinary Parasitology (WAAVP). 4-8 September, 2017, Kuala Lumpur Convention Centre, Malaysia |
| 7. | Mentor. Ungku Omar-Newton Fund Researcher Workshop: Neglected Diseases in SEA: Building Capacity in Epidemiological Modelling. 28 August – 1 September, 2017, Institute of Biological Sciences, Faculty of Science, University of Malaya |
| 8. | Scientific Advisory Board for The Vietnam Annual National Scientific Conference on Infectious Diseases and HIV/AIDS & 8th ASEAN Congress of Tropical Medicine and Parasitology (ACTMP) 2018. 27-29 July, 2018 in Nha Trang, Khanh Hoa, Vietnam |
| 9. | Assistant Editor of Tropical Biomedicine, ISI journal published by Malaysian Society of Parasitology and Tropical Medicine |
| 10. | Editorial board of Food and Waterborne Parasitology |

National

| No | Role |
|----|--|
| 1. | Honorary Lecturer (Parasitology), Faculty of Medicine, UiTM Session 2012/2013-2013/2014 |
| 2. | Chairperson of the Scientific Committee of the 49 th Annual Scientific Conference of the Malaysian Society of Parasitology and Tropical Medicine, 19 – 20 March 2013, Grand Seasons Hotel, Kuala Lumpur |
| 3. | President of the 50 th Malaysian Society of Parasitology and Tropical Medicine 2014/2015 Council |
| 4. | Chairperson of the Organising Committee of the 51 st Malaysian Society of Parasitology and Tropical Medicine Annual Scientific Conference, 3-4 March 2015, Grand Seasons Hotel, Kuala Lumpur |
| 5. | Selection Board of the Malaysian Society of Parasitology and Tropical Medicine Nadchatram Medal for the 52 nd MSPTM Annual Scientific Conference 2016 |
| 6. | Member of the Scientific Committee of the 52 nd Annual Scientific Conference of the Malaysian Society of Parasitology and Tropical Medicine, 2-3 March 2016, Grand Seasons Hotel, Kuala Lumpur |
| 7. | Council Member of the 51 st Malaysian Society of Parasitology and Tropical Medicine 2015/2016 Council |
| 8. | Fellow of the Academy of Sciences Malaysia (ASM) |
| 9. | Vice Chairperson of the Scientific Committee of the 54 th Malaysian Society of Parasitology and Tropical Medicine Annual Scientific Conference, 14-15 March 2018, Capri, Bangsar South, Kuala Lumpur |

SELECTED INVITED SPEAKER**International Conference/Workshop**

| No | Activity | Title presented | Organiser | Start | End |
|----|--|---|--|----------|----------|
| 1. | VIIIth National Conference of the Indian Academy of Tropical Parasitology (IATP) | Novel diagnostic tools for emerging zoonotic parasites in Southeast Asia | Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India | 6/9/13 | 8/9/13 |
| 2. | 2 nd ASEAN Workshop and 19 th Biological Sciences Graduate Congress (BSGC), National University of Singapore | How are helminthes, asthma and allergy associated? | National University of Singapore | 11/12/14 | 13/12/14 |
| 3. | Neglected Tropical Diseases Symposium Speaker. 6 th ASEAN Congress of Tropical Medicine and Parasitology and 50 th Malaysian Society of Parasitology and Tropical Medicine | Addressing key issues of soil transmitted helminthiasis in Orang Asli (indigenous) communities with modern technologies | 6 th ASEAN Congress of Tropical Medicine and Parasitology | 5/3/14 | 7/3/14 |
| 4. | World Expert Lecture Series of the Office of Vice President for Academic Affairs, University of the Philippines | Novel molecular tools for rapid detection of zoonotic pathogens in Southeast Asia | University of the Philippines | 10/3/16 | 10/3/16 |
| 5 | Food and Water-Borne Parasites: From Production to Consumption Seminar | Connecting water to food: a focus on pathogenic parasites | Southern Luzon State University, Philippines | 11/3/16 | 11/3/16 |

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| 6. | Keynote speaker of the conference by the Philippines Society of Parasitology Annual Conference, 8 th Scientific Meeting | Responding to the challenges in the elimination of neglected tropical diseases | Philippines Society of Parasitology | 12/3/16 | 12/3/16 |
| 7. | 7 th ASEAN Congress of Tropical Medicine and Parasitology and 3 rd International Conference on Molecular and Clinical Aspects of HIV-AIDS, Tuberculosis and Malaria | Helminths and gut microbiota: What's the connection? | 7 th ASEAN Congress of Tropical Medicine and Parasitology, Malang, Indonesia | 17/5/16 | 19/5/16 |
| 8. | Ungku Omar-Newton Fund Researcher Workshop: Neglected Diseases in SEA: Building Capacity in Epidemiological Modelling | International grant calls for infectious disease research in Southeast Asia | Ungku Omar-Newton Fund Researcher Workshop | 28/8/17 | 1/9/17 |
| 9. | International Association for Food and Waterborne Parasitology (IAFWP) Symposium. 26 th International Conference of the World Association for the Advancement of Veterinary Parasitology (WAAVP) | Waterborne and foodborne parasites in Southeast Asian countries | 26 th International Conference of the World Association for the Advancement of Veterinary Parasitology (WAAVP) | 4/9/17 | 8/9/17 |

National

| No | Activity | Title presented | Organiser | Start | End |
|----|--|--|--|---------|---------|
| 1. | Workshop on prevalence of cryptosporidiosis and giardiasis in drinking water | Cryptosporidiosis and Giardiasis in Southeast Asia: An emphasis on Malaysia | MyoHUN (Malaysia One Health University Network) and USAID | 1/4/14 | 2/4/14 |
| 2. | Program Pembelajaran Berterusan Seksyen Kawalan Alam Sekitar, Bahagian Perkhidmatan Kejuruteraan, Kementerian Kesihatan Malaysia | <i>Cryptosporidium</i> oocysts and <i>Giardia</i> cysts in Malaysia | Seksyen Kawalan Alam Sekitar, Bahagian Perkhidmatan Kejuruteraan, Kementerian Kesihatan Malaysia | 9/5/14 | 9/5/14 |
| 3. | Hospital Orang Asli Gombak | Improving the health status of the Orang Asli: From parasitic infections perspective | Hospital Gombak, Ministry of Health | 28/4/15 | 28/4/15 |
| 4. | Mesyuarat Penilaian Pencapaian Program Community Feeding Tahun 2015, Hotel Lexis, Port Dickson, Negeri Sembilan. | Parasitic infections and malnutrition among the Orang Asli | Ministry of Health | 7/10/15 | 7/10/15 |

SELECTED AWARDS

1. Academy of Sciences Malaysia (ASM) Fellow, Academy of Sciences Malaysia, 2017 (National)
2. Certificate of Excellent Service, University Malaya, 2016 (University)
3. Top Research Scientists Malaysia 2016, Academy of Sciences Malaysia, 2016 (National)
4. Excellence Service Award, University Malaya, 2015 (University)
5. UM Excellence Awards 2015 - Excellent Lecturer, University of Malaya, 2015 (University)
6. Certificate of Excellent Service, University Malaya, 2014 (University)
7. Excellence Service Award, University Malaya, 2012 (University)
8. Gold Medal in Seoul International Invention Fair (Siif) 2012, Seoul, Korea, 29th November to 2nd December, Korean Invention Promotion Association, 2012 (International)
9. Most Promising Innovation Award in BioMalaysia 2012, Kuala Lumpur Convention Centre, Kuala Lumpur, 5-7 November 2012, Ministry of Science, Technology and Innovation, 2012 (National)
10. Gold Medal in BioMalaysia 2012, Kuala Lumpur Convention Centre, Kuala Lumpur, 5-7 November 2012, Ministry of Science, Technology and Innovation, 2012 (National)
11. Certificate of Excellent Service, University Malaya, 2011 (University)
12. Gold Medal in BioMalaysia Exhibition 2011, Kuala Lumpur, 21-23 November 2011, Ministry of Science, Technology and Innovation, 2011 (National)
13. Silver Medal in Malaysia Technology Expo 2011, Kuala Lumpur, 17-19 February 2011, Malaysian Association of Research Scientists, 2011 (National)
14. Gold Medal in BioMalaysia Exhibition 2010. Kuala Lumpur Convention Centre, 1-3 November 2010, Ministry of Science, Technology and Innovation, 2010 (National)
15. Certificate of Excellent Service, University Malaya, 2009 (University)
16. Excellence Service Award, University Malaya, 2008 (University)
17. Royal Society of Tropical Medicine and Hygiene Centenary Scholarship, Royal Society of Tropical Medicine and Hygiene (London), 2008 (International)
18. Malaysian Society of Parasitology and Tropical Medicine Award, Malaysian Society of Parasitology and Tropical Medicine, 2007 (National)

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My husband, Dr Benedict Sim for his unwavering love, faith, patience, understanding and being my pillar of strength throughout my entire career. John Paul, Joseph and Joachim, my three heroes, you are my sources of inspiration and motivation. Thank you for bringing so much joy and meaning to our lives.

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Most importantly, I praise and thank Almighty God for His bountiful blessings.

University of Malaya

In my quest to unravel science, I learned that team effort is one of the utmost important ingredients to excel in the discovery of science.