USM-RIKEN INTERNATIONAL CENTER FOR AGING SCIENCE

Impact Report | 2015-2021

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This report was compiled by A.S. Navanithan.

Layout and editing by Eugene Ong.

FOREWORD

The USM-RIKEN International Center for Aging Science (URICAS) was conceptualised in January 2014 with the intention to firstly, bring together the many USM researchers who had worked together with RIKEN in their one-to-one research collaborations, and to secondly, reciprocate the generous support RIKEN has provided in training many of our USM students since the acceptance of the first USM student as an Asia Program Associate in 2001.

The URICAS program aimed to formalise the various USM-RIKEN research groups under a single focus of ageing, to work together as a cluster to tackle ageing topics at the fundamental level. While it had initially focused on fundamental life sciences to study the ageing problem from the cellular and organismal perspective, it had also expanded in USM to include the social sciences with a focus on the elderly's health promotion behaviors.

"Curiosity, passion and connections are crucial.
To make a breakthrough in science, you need serendipity.
Friends are important;
an important field cannot be explored by one person alone."

— Noyori Ryoji

As with prior USM-RIKEN collaborations, the URICAS program was made possible by the full support from both USM and RIKEN from the top managements to the researchers and students, culminating in research outputs (publications, patents, awards), mentoring and training of the next generation researchers (URICAS Youngsters), and a foothold in the community through various initiatives including the Penang state-supported International Conference on Ageing 2019. This report serves as record of our impact and activities from 2015 until 2021.

Thank you.

PROFESSOR SHAHARUM SHAMSUDDIN
COORDINATOR
USM-RIKEN INTERNATIONAL CENTER FOR AGING SCIENCE

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1.0 USM-RIKEN BACKGROUND

The relationship between University Sains Malaysia (USM) and RIKEN was initiated in 1993 when USM researchers (Dr Mohamed Isa Abd Majid, Dr Mohd Nazalan Mohd Najimudin and Dr Mohd Razip Samian) were welcomed by RIKEN as visiting scientists at the Polymer Chemistry Laboratory.

This successful initial attachment was followed up by the independent graduate study of K. Sudesh Kumar from 1995 to 2001, also at the Polymer Chemistry Laboratory, RIKEN, first as a graduate student and subsequently as a postdoctoral researcher. In part, based on the positive experiences of Dr Sudesh as a graduate student at RIKEN, the Joint Graduate School Program (APA) agreement between RIKEN and USM was formally signed in 2001. The APA programme and its successor programme, International Program Associate (IPA) signed in 2008, became the stepping-stone for many additional doctoral candidates to enrol at RIKEN institutes. A key aspect of the APA and IPA programmes was that students conduct their research activities at RIKEN laboratories under their respective laboratory hosts, while the doctoral degrees were awarded by USM.

As the years passed on, additional Memorandums of Understandings (MOU) were signed between USM and RIKEN further enhancing knowledge exchange and spurring joint research activities. To date, more collaborative efforts have been established between USM and RIKEN, thus fostering extensive knowledge exchange and human capital development (Figure 1).

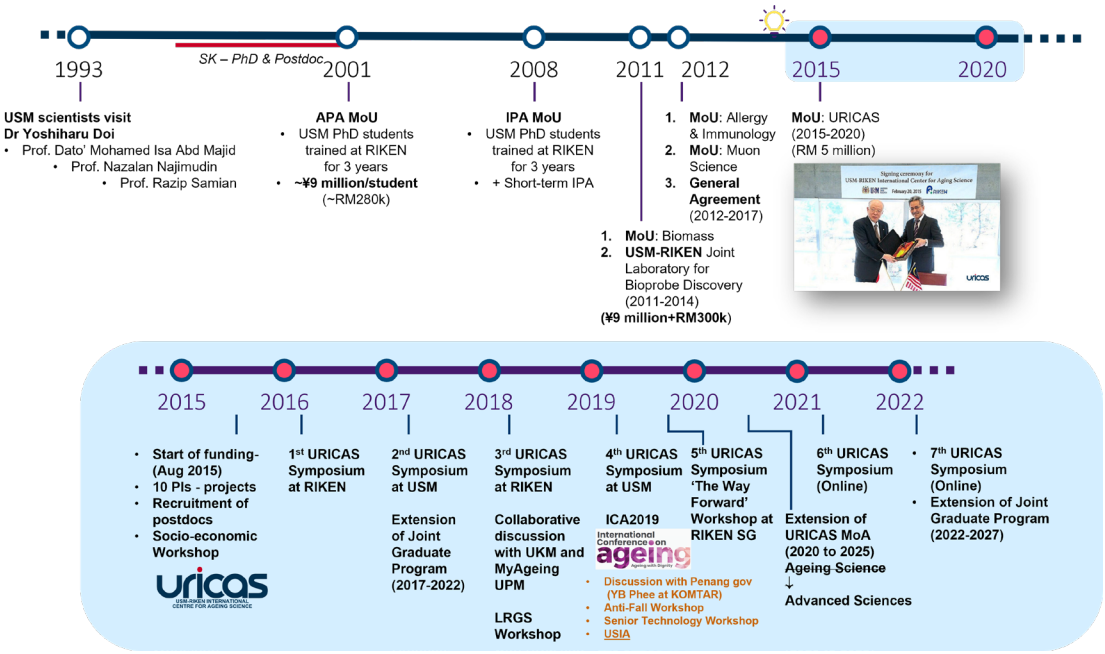

Figure 1: Historical timeline of the USM-RIKEN collaboration.

1.1 Joint Graduate Program between USM and RIKEN

This programme was initiated in 2001 under the name Asian Program Associate (APA). The main purpose is to identify and foster talented young scientists capable of contributing future research collaborations between USM and RIKEN. The programme is for PhD students registered at USM. USM students selected under this programme will execute research at RIKEN for up to a maximum period of 3 years. Upon successful completion, students will be conferred a PhD degree by USM and a certificate by RIKEN attesting to their completion of the joint programme.

1.2 RIKEN

RIKEN is one of Japan's largest research organizations with branch institutes and centres in various locations throughout Japan. RIKEN's more than 3000 researchers publish several hundred research articles in top scientific and technical journals every year across a broad spectrum of disciplines in physics, chemistry, biology, medicine, engineering and in many areas of technology.

1.3 The Coordinator

In order to ensure the sustainability of the IPA programme, the Vice-Chancellor of USM officially appointed Prof. Dr K. Sudesh Kumar as the coordinator of this programme for USM. Among his responsibilities are to monitor the progress of the PhD students and to further strengthen the research and academic collaboration with RIKEN scientists. Prof. Sudesh is very familiar with RIKEN and its administrative system due to his long personal affiliation with RIKEN. He was a Monbusho scholar from 1995 to 1999 during his graduate doctoral research at the Polymer Chemistry Laboratory, RIKEN. His PhD supervisor Prof. Yoshiharu Doi, who is currently a senior administrative staff of RIKEN, was more than happy that Prof. Sudesh joined his laboratory again for two years as a postdoctoral researcher. With this broad experience as a student and also as a researcher at RIKEN, Prof. Sudesh is not only very familiar with the RIKEN system, but also well connected with many of the senior and junior administrators as well as scientists. Most importantly, he understands the work culture of Japanese researchers as well as the demands and expectations placed on IPA students. The experience allows him to select the best candidates for the programme and to prepare and motivate them for their attachment at RIKEN.

1.4 Impact

The USM-RIKEN Joint Graduate School Program has far-reaching short-term and long- term national and international impacts. The immediate short-term impact can be seen in the exposure given to USM's students. The high-level fundamental research carried out at RIKEN as well as the advanced facilities provide them with extensive opportunities to learn and master new knowledge and research skills. In addition, the

students are also indirectly exposed to the Japanese language and culture. The programme provides valuable opportunities for the students who are interested to learn a new language as well as to get acquainted with the work ethics of the Japanese people.

RIKEN scientists are comprised of both Japanese and non-Japanese world-class scientists. Therefore, RIKEN also provides the students with the opportunities to interact with leading international scientists from a variety of nationalities. As a result, the students have many opportunities to form their own research networks, which will be important for their career development in the future.

Besides direct exposure to students, RIKEN actively promotes collaborative efforts with USM and Malaysia via various high impact initiatives. In 2009, the 2nd International Conference on Bio-based Polymers was held at USM. The conference was jointly organized and funded by USM, RIKEN and the University of Tokyo. The conference brought together, for the first time in Malaysia, world-renowned experts in the field of bio-based and biodegradable polymers. The conference focused on the development of environmentally friendly materials to ensure a sustainable tomorrow.

In 2007, RIKEN awarded Malaysia's ex-Prime Minister, Tun Dr Mahathir Mohammad the prestigious RIKEN Honorary Fellow for his strong commitment to develop science and technology in Malaysia (Figure 2). During this historic event, USM was invited to showcase the exemplary strong research collaboration between RIKEN (Japan) and USM (Malaysia).

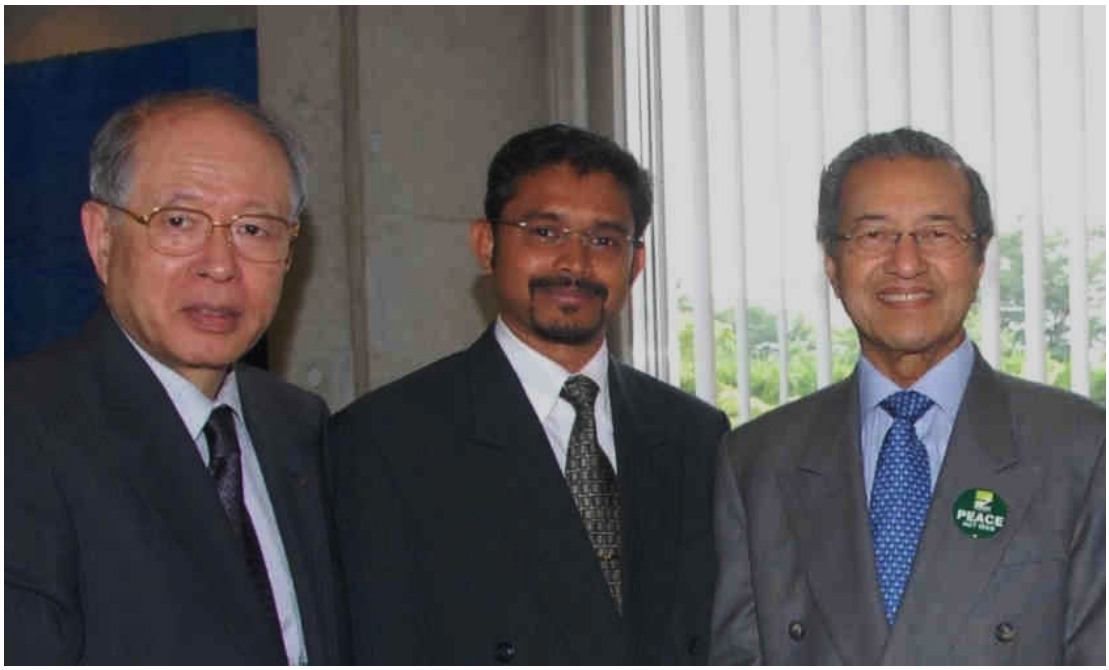

Figure 2: Prof. Dr Ryoji Noyori (Nobel Laureate in Chemistry and President of RIKEN), Prof. Dr K. Sudesh Kumar (USM) and Tun Dr Mahathir Mohammad (former Prime Minister of Malaysia) during the prestigious RIKEN Honorary Fellow award-giving ceremony at RIKEN, Japan.

USM and RIKEN already had very strong research ties before the start of this Joint Graduate Program. RIKEN had hosted several researchers from USM in order to establish research collaborations. Most of the early research activities centred on the development of bioplastics with the School of Biological Sciences. Prof. Yoshiharu Doi has been instrumental in starting many of the research collaborations with USM. Therefore, in August 2006, USM conferred an Honorary Doctorate to Prof. Doi, who together with RIKEN's President, Prof. Ryoji Noyori is a member of the International Advisory Board of USM. In 2011, USM conferred another Honorary Doctorate, this time to the President of RIKEN, Prof. Ryoji Noyori.

1.5 APA/IPA programme student numbers

To date, a total of 28 long-term (stay up to 3 years) IPA students and 21 short-term (stay less than 12 months) students conducted research under the IPA programme since 2011 (Figure 3). Additionally, 3 APA students joined RIKEN from 2002 to 2007. In total, 52 students were exchanged under the APA/IPA programme.

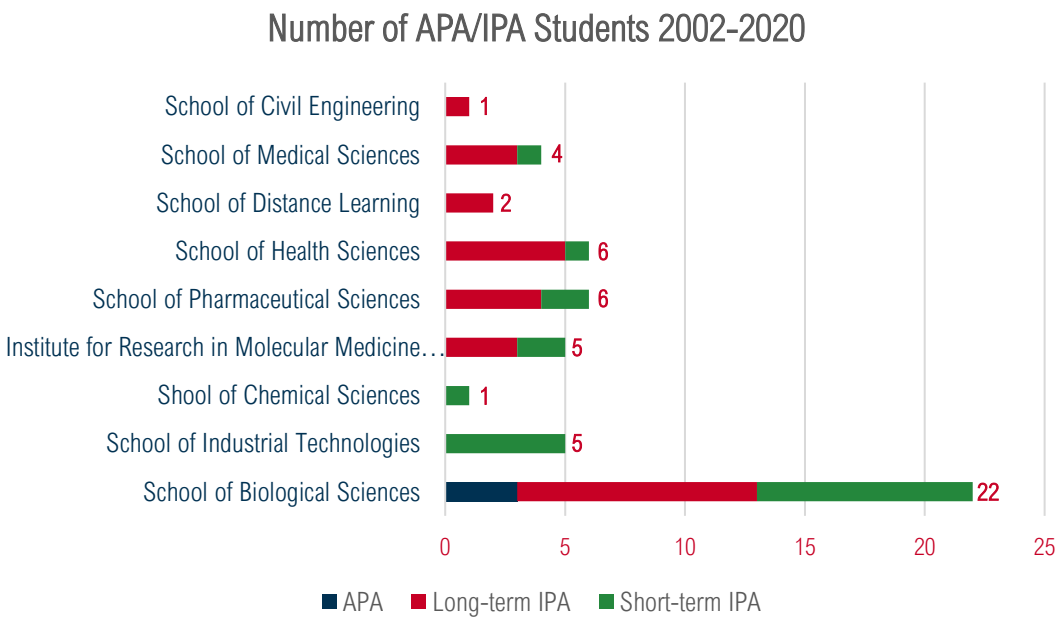

Figure 3: The number of APA/IPA students from Joint Graduate Program between USM and RIKEN since 2002 to 2020. (Updated December 2020)

In this context, it is vital to highlight that the continued success of the joint USM-RIKEN programme is based on its ability to grow, not only in terms of number of students, but more importantly in the number of USM schools and RIKEN host laboratories involved. Today, 9 different schools at USM and 7 different centres at RIKEN are actively involved, demonstrating the scientific width of the USM-RIKEN collaboration.

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host laboratories involved. Today, 9 different schools at USM and 7 different centres at RIKEN are actively involved, demonstrating the scientific width of the USM-RIKEN collaboration.

1.6 Financial support by RIKEN for the USM-RIKEN collaboration (2015-2020)

In addition to providing a place for students to learn and hone their research skills, RIKEN has also contributed financially to the USM-RIKEN collaboration. On top of living allowance, RIKEN provides housing financial aid, insurance as well as International SOS service to USM students during their stay in Japan throughout their APA/IPA period. Other benefits that were offered to students include access to high quality research facilities and equipment, child-care facilities and libraries as well as opportunities to participate in multi-disciplinary, multi-cultural net-working events such as the Discovery Evening, RIKEN Summer School and Interdisciplinary Exchange Evening. In total, RIKEN has spent a total of RM 3,109,611.33 (¥79,856,480) for USM students from the year 2015 to 2020 (Table 1 and Figure 4).

Table 1: Total expenses paid by RIKEN for USM-RIKEN students in years 2015 to 2020.

FY2015	FY2016	FY2017	FY2018	FY2019	FY2020	International SOS Service	TOTAL COST
¥20,787,343	¥8,201,612	¥12,608,761	¥13,335,888	¥16,667,026	¥7,965,850	¥290,000	**¥79,856,480**
RM 809,459	RM 319,370	RM 490,985	RM 519,299	RM 649,013	RM 310,190	RM 11,292	**RM 3,109,611**

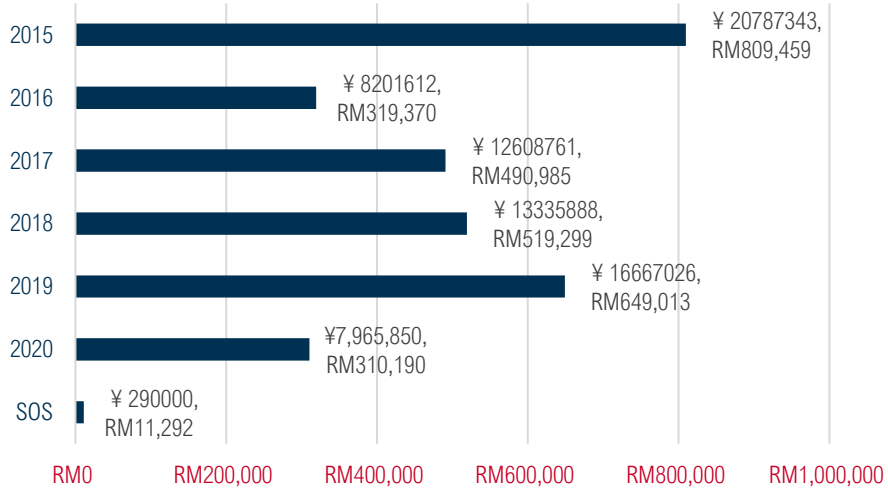


Figure 4: Estimated expenses paid by RIKEN for USM-RIKEN students (2015-2020).

In addition to this, individual RIKEN PIs and laboratories have also spent on other (hidden) costs such as laboratory consumables, equipment fees as well as travel and meeting fees. An estimated ¥1,500,000 (~RM 50,000) is invested in an IPA student per year in their host laboratories.

Table 2: Other Costs (Per student per year).

Type	Sum
Consumables	¥1,000,000 (RM 30,000)
Equipment fees	¥350,000 (RM 11,500)
Travel/meeting fees/other	¥150,000 (RM 4,950)

1.7 Other USM and RIKEN Collaborations

Besides the Joint Graduate Program, USM and RIKEN have also established a variety of other joint programmes and laboratories.

1.7.1 USM-RIKEN Joint Laboratory for Drug Discovery

The joint laboratory focusing on Drug Discovery was established in 2011 and was headed by Prof. Habibah Wahab, who is currently the Chief Executive Director of Institute of Pharmaceutical and Nutraceutical (IPHARM). Her counterpart in RIKEN was Prof. Hiroyuki Osada, who is currently the Deputy Director at the RIKEN Center for Sustainable Resource Science and Unit Leader of the Drug Discovery Platforms Cooperation Division.

1.7.2 Genomics Research

Another area of research with ongoing collaboration with RIKEN is on genomics. RIKEN's advanced computing facilities and technical skills enable the processing of large quantities of complex genetic information. Researchers and students from the School of Industrial Technology as well as the School of Biological Sciences are currently working with RIKEN on various projects related to microbial genomics.

1.7.3 Brain Science Research

As of late, USM and RIKEN are discussing to further expand the Joint Graduate Program to provide training as well as to jump-start USM's Brain Science Program with the help of RIKEN's world-renowned Center for Brain Science. It is hoped that this Joint Graduate Program will eventually lead to the setup of a joint research laboratory or research centres at USM; allowing short-term dispatchment of RIKEN scientists to carry out collaborative research and provide training at USM, Malaysia. To ensure the continuity of such collaborative efforts, RIKEN has officially appointed Prof. Sudesh as an Administrative Advisor of RIKEN. Among his duties are to provide advice to RIKEN on the promotion of cooperation between RIKEN and research institutions in Asia, including Malaysia, and to coordinate such cooperation.

2.0 URICAS

USM-RIKEN Centre for Ageing Science was established as a collaborative programme by Universiti Sains Malaysia (USM) and RIKEN, Japan, to undertake research on ageing and illnesses associated with the process of ageing. A memorandum of understanding was signed between USM and RIKEN on 20th February 2015, setting out the development of URICAS. USM was represented by Vice-Chancellor, Prof. Dato' Dr Omar Osman, and RIKEN's President at the time of signing, Prof. Dr Ryoji Noyori. This event signified almost two decades of relationship of collaborative research between RIKEN and USM. As mentioned by Prof. Noyori, it was hoped that this particular relationship between USM and RIKEN would be the starting point towards identifying solutions to end the problem of ageing faced by globally.

Ageing is a natural process concerning physiological, cellular as well as social changes of an organism over a period of time. URICAS promotes advanced research on ageing to understand its basics as well as its biological and social consequences. This research programme on ageing science would also provide the space and opportunity for young researchers from both countries to be involved in ageing research. Dato' Prof. Omar Osman, USM Vice-Chancellor, believed that the establishment of URICAS would provide benefits not only to researchers, but also to mankind, for this research collaboration is aimed at the global community.

This collaborative programme will develop to provide a platform and opportunities specifically to young researchers from both countries to be intensively involved in basic and applied research. As such, one of the main objectives of the formation of URICAS is on the training of bright young researchers and to create an incubation space for graduates of the joint USM-RIKEN APA/IPA programme to further develop their career as post-doctoral researchers at both USM and RIKEN. This represents the next step of the long-term goal to further deepen and simultaneously broaden the USM-RIKEN collaboration.

On the 25th of June 2020, an agreement to continue this research collaboration was signed by USM's Vice-Chancellor, Prof. Dr Faisal Rafiq Mahamd Adikan and RIKEN's executive director Prof. Dr Harayama Yuko. As such, the URICAS collaboration between both parties was extended to February 24th, 2025. The agreement recognizes the frequent and significant research exchange in various research fields between RIKEN and USM, the fruitful activities of the USM-RIKEN Joint Laboratory for Bioprobe Discovery at INFORMM as a centre for chemical biological research in South Asian countries, the strong desire of both USM and RIKEN to make efforts in nurturing young scientists through their collaboration as well as the mission of both USM and RIKEN to contribute to the international society including Asia by promoting further collaboration for the advancement of research and development. As such, both parties have agreed to cover a broader range of scientific fields, not limited to Aging. To reflect this change, the unabbreviated name of URICAS shall be changed from 'USM-RIKEN International Center for Aging Science' to 'USM-RIKEN Interdisciplinary Collaboration for Advanced Sciences'.

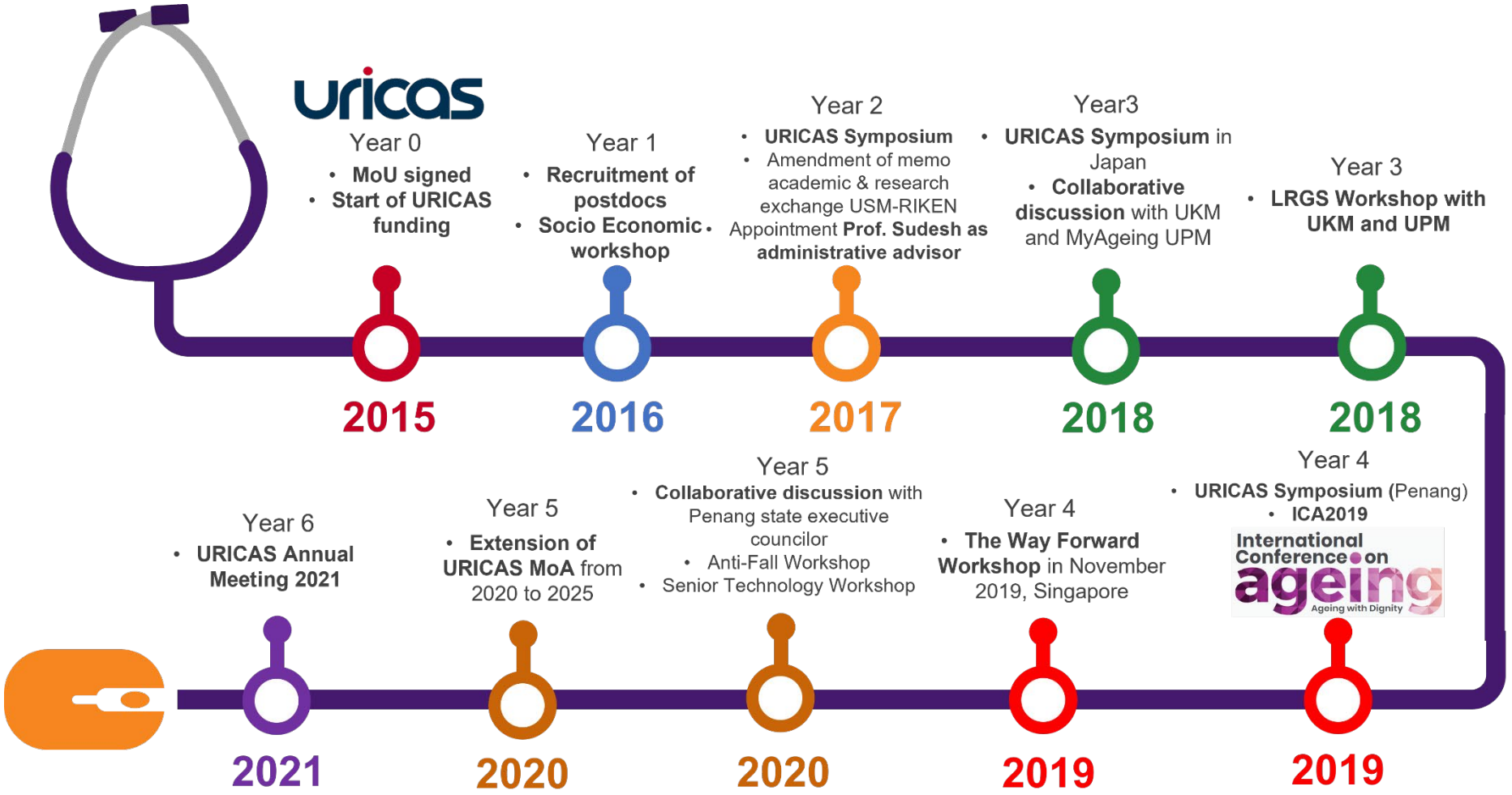


Figure 5: Overview of URICAS activities 2015-2021.

2.1 Objectives of URICAS

As briefly indicated in the 'Background' section, the URICAS collaboration effort between USM and RIKEN is based on the following equally important cornerstones:

- Advancing basic and applied research on science
- Expanding scope (involved centres and schools) of USM-RIKEN collaboration
- Broadening scientific collaboration between USM and RIKEN
- Streamlining the identification and recruitment of promising students for the short- and long-term IPA programme
- Creating post-IPA career opportunities and support environments for selected IPA graduate candidates
- Promoting frequent and significant research exchange between USM and RIKEN

2.2 URICAS teams

URICAS comprises 12 teams. The teams cover a broad scope of disciplines ranging from genetics to physics as well as social sciences. As such, each have their unique approach in solving ageing issues. Regardless, the 12 teams also work hand-in-hand with each other to support the objectives of URICAS.

Prof. Dr Shaharum Shamsuddin | Dr Kuniya Abe
Identification of CTCFL Downstream Targets in Physiological and Aberrant States

Prof. Dr Liong Min Tze | Prof. Dr Hiroshi Ohno
Investigation of Probiotic Benefits in Human Health

Prof. Dr Habibah A. Wahab | Dr Hiroyuki Osada | Dr Toshihiko Nogawa
Catalogue of USM-RIKEN Natural Product (CURINaP) Library for the Discovery of Bioactive Molecules on Ageing and Ageing Related Diseases

Prof. Dr Gam Lay Harn | Dr Peter Greimel
Protein, Metabolite and Lipid Profile in T2DM (Type 2 Diabetic Mellitus) Rat Models upon High Plant Fat Diet Intake

Prof. Dr K. Sudesh Kumar | Dr Keiji Numata | Dr Hideki Abe
Development of New Biopolymers for Medical and Therapeutic Applications in Aged Patients

Assoc. Prof. Dr Badrul Hisham Yahaya | Dr Mitsuru Morimoto
The Anti-senescence Effects of Mesenchymal Stem Cells (MSC)-Derived Extracellular Vesicles (Evs) on COPD

Prof. Dr Nazalan Najimudin | Assoc. Prof. Dr Ghows Azzam | Dr Nobumoto Watanabe
Synthetic Compounds Screening for Alzheimer's Disease using Drosophila melanogaster

Prof. Dr Shukri Sulaiman | Prof. Dr Isao Watanabe
Understanding Electron Transport in DNA: μSR and First-Principle Computational Investigations

Dr Teh Aik Hong | Dr Tamao Hisano
mTOR Signalling

Dr Eugene Ong | Dr Nobumoto Watanabe
Ageing Studies in Yeast Saccharomyces cerevisiae

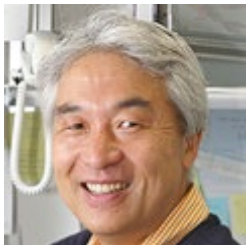
Prof. Dr Phua Kia Kien | Assoc. Prof. Dr Aziah Ismail | Dr Todd Taylor
Transcriptome study of biofilm formation in Salmonella enteric subspecies enteric Serovar Typhi in the aged

Assoc. Prof. Dr Saidatulakmal Mohd
Health Promotion Behaviour of Elderly

Identification of CTCFL Downstream Targets in Physiological and Aberrant States

Team leaders

Prof. Dr Shaharum Shamsuddin
Universiti Sains Malaysia
School of Health Sciences



Dr Kuniya Abe
RIKEN
BioResource Research Center

Team members

- Maisarah Ab Samad
- Dr Daruliza Kernain Mohd. Azman

Scientific background

Multiple regulatory elements work together to mediate tissue-specific gene regulation. Binding of transcription factors to cis-elements causes regulatory interactions which control the transcriptional activity of the downstream target genes, thereby ensuring tissue-specific gene expression profiles. Occurrence of illegitimate gene expression may be harmful for cellular status. For example, aberrant expression of tissue-restricted genes such as testis-specific genes or cancer/testis antigen (CTA) genes is frequently observed in many types of cancer. Testis-specific CTCF-like or Brother of the Regulator of Imprinted Sites (CTCFL/BORIS) is the paralog of ubiquitous architectural factor, CTCF. CTCFL binding largely overlaps with CTCF binding sites due to the shared zinc finger domain. CTCFL is known to be expressed in many tumor cell types as well as normal male germ cells and known to play essential roles in mouse spermatogenesis. Yet, its role as a transcriptional regulator in the male germ cells is still unclear. Aberrant expression of CTCFL outside the germ cells might rewire the transcriptional programme and induce germline expression programme in somatic cells, which may cause genome instability leading to tumor development.

Project aim

Here we aim to investigate effects of induced CTCFL expression on both germ cells and non-germ cells and to identify molecular targets of CTCFL in these cells. To examine effects of ectopic expression CTCFL, conditional 3xFLAG-CTCFL transgene was introduced to non-germ cells; the mouse embryonic stem (ES) cells, differentiating mouse embryoid bodies and JK-1 testicular stroma cell line [Aberrant state]. To silence the endogenous CTCFL in male mouse germline stem cells, we used RNA interference technique (by using DsiRNA) [Physiological state]

By combining our gene expression profiling and the published CTCFL binding sites data, we identify molecular targets of CTCFL and discuss mechanism of CTCFL- dependent regulation of gene expression in spermatogenesis and cancer.

Executive summary of research results

The global expression profiling data suggested that effects of ectopic CTCFL expression in non-germ cells are predominantly cell-context dependent. Deregulated genes found in these cell types were not largely overlapped. Germline genes known to be direct targets of CTCFL such as Prss50, Stra8 and Gal3st1are indeed upregulated in undifferentiated ES cells, but not in embryoid bodies and in JK1 cells. Distinct sets of genes are upregulated in JK1 upon induction of CTCFL expression. Interestingly, although not overlapping with upregulated genes in ES, some of the induced genes in JK1 or embryoid bodies show predominant expression in testis or brain. Only one gene,

i.e. Adgrg1 is upregulated commonly by CTCFL in all the samples tested. Adgrg1 encodes GRP56 (G protein-coupled receptor 56) protein, a member of the adhesion GPCR family. Adgrg1 is expressed in many tissues and organs and known to have roles in cell guidance/adhesion in tumor inhibition or in neural development and to be involved in testis development and in male fertility.

The reason why the CTCFL ectopic expression results in deregulations of distinct sets of genes in the different cell types is not understood at this moment. Manipulations of undifferentiated ES cells often result in deregulations of genes normally expressed in early embryos or germ cells, which is also the case for CTCFL ectopic expression. On the contrary, JK1 or cells in the embryoid bodies undergo a series of epigenetic changes in the process of differentiation, thereby establishing epigenomic status more resistant for the CTCFL expression.

Short term outlook (upcoming publications/results)

We are now validating the deregulated genes by RT-qPCR and checking the CTCFL binding in the ChIP-seq analysis.

Future direction of joint research

A knock-down experiment on CTCFL in the male germline stem cells is now underway. The expression changes from the CTCFL knockdown should be useful for identification of downstream targets of CTCFL in male germ cells. Knowledge on the germline-specific gene regulation by CTCFL should lead to better understanding of the cell fate changes in spermatogenesis and in cancer.

Student training and fostering of future academic leaders

- Maisarah Ab Samad, PhD graduate at School of Health Sciences, USM Health Campus, 16150 Kubang Kerian Kelantan
- Nurul Fatihah Mohamad Nasir, PhD candidate at School of Health Sciences, USM Health Campus, 16150 Kubang Kerian Kelantan
- Scientific results Published and accepted manuscripts in refereed journals
- Nurul Fatihah Mohamad Nasir; Azalina Zainuddin; Shaharum Shamsuddin. 2018. Emerging Roles of Sirtuin 6 in Alzheimer's Disease. Journal of Molecular Neuroscience.
- Nor Shaheera Mohamad Kamal, Sabreena Safuan, Shaharum Shamsuddina, Parisa Foroozandeh. 2020. Aging of the cells: Insight into cellular senescence and detection Methods. European Journal of Cell Biology.
- Parisa Foroozandeh, Siti Asmaa Mat Jusoh, and Shaharum Shamsuddin. 2021. Passive Drug Delivery, Mechanisms of Uptake, and Intracellular Trafficking. In L.S. Milane & M.M. Amiji, (Eds), Organelle and Molecular Targeting (pp. 129-152). CRC Press.

Oral presentations

- Generation of pcDNA3.1-P301L Tau for the development of in vitro model of Alzheimer's disease, URICAS Symposium 2017
- Effect of different percentage of serum in the differentiation media of SH SY5Y cell line towards its dendritic length, URICAS Symposium 2018
- Human P301L-Tau: possible role in neuritogenesis and pre-synapse formation in differentiated stably mutated SH-SY5Y cell, URICAS Symposium 2019
- Human P301L-Tau impaired neuritogenesis and pre-synapse formation in differentiated stably mutated SH-SY5Y cell, International Conference on Ageing 2019 (ICA 2019)
- Serum Affects Differentiation of SH SY5Y Cell Line with Regard to Dendritic Length and Expression of Neuron Specific β-III Tubulin, ASEAN Emerging Researchers Conference 2019

Investigation of probiotic benefits in human health

Team leaders

Prof. Dr Liong Min-Tze
Universiti Sains Malaysia
School of Technology Industry

Dr Hiroshi Ohno
RIKEN
Center for Integrative Medical Sciences

Team members

- Ahmad Imran Zaydi; Research Officer, USM
- Goh Wei Chiang; Research Officer, USM
- Fiona Chung Yi Li; Research Officer, USM
- Naoko Satoh-Takayama, PhD, Senior Research Scientist, RIKEN
- Takashi Kanaya, PhD, Senior Scientist, RIKEN
- Yumiko Nakanishi, PhD, Senior Scientist, RIKEN
- Tamotsu Kato, PhD, Senior Scientist, RIKEN
- Eiji Miyauchi, PhD, Senior Scientist, RIKEN
- Takaharu Sasaki, PhD, Senior Scientist, RIKEN
- Takashi Ito, MD/PhD, Postdoctoral Researcher, RIKEN

Scientific background

We are committed in development of probiotics and/or prebiotics as neutraceuticals and health potentials of bioactive materials and components from probiotics. We are currently undergoing experiments about probiotics Lactobacillus DR7 and Lactobacillus DR9 in human health. We are also studying the molecular mechanisms of the impact of gut microbiota on diseases.

Gut is one of the largest lymphoid organs in our body harbouring approximately 4 trillion of bacteria (Sender et al., 2016). Weighing about 1- 2 kg, the gut microbiota is constituted of 1000 bacterial species encoding not less than five million genes (D'Argenio and Salvatore, 2015). Therefore, gut microbiota is also referred as the second genome (Grice and Segre, 2012). As gut microbiota control host physiology and survival, the roles of these bacteria in the aging process are indispensable. Aging is irreversible and inevitable, but the onset of age-related disorders can be delayed/ prevented through a healthy, balanced lifestyle- a term known as healthy aging.

Probiotics such as those from the genus of Lactobacillus have been shown to improve blood lipid profile in animal studies. Studies have shown that several Lactobacillus strains were able to reduce total cholesterol (TC) and triglyceride (TG) concentrations in rats [2]; Xie et al., 2011). A recent systematic review and a meta- analysis of 15 randomized controlled trials reported that probiotics consumption was able to decrease total-cholesterol and LDL-cholesterol levels effectively (Wu et al., 2017).

Increasing evidence has shown the association of gut microbiota with brain health along the gut-brain axis, a bidirectional flow of signalling responses between the gut and brain (Mayer, 2011). Microbial neuroactive substances and their precursors such as tryptophan have been reported to reach the brain through

endocrine and afferent autonomic pathways leading to altered behavioural responses (Desbonnet et al., 2008), and brain development, mood and cognition (Romijn et al., 2008).

Project aim

- To investigate the potential effect of the probiotic in hyperlipidemia, liver steatosis, aging and brain function.
- To evaluate healthy aging effect of selected probiotics
- To perform premature-senescence induction on selected
- To evaluate in-vitro of selected LAB metabolites on aged cell lines
- To investigate of mechanism of selected LAB metabolites on aged cell lines.
- To identify and characterize metabolites Completed
- To investigate anti-aging effect of selected LAB metabolites in-vivo model
- Product development and assessment

Executive summary of research results

- Lactobacillus has the potentials as a promising natural intervention to alleviate cardiovascular, liver diseases, aging and improve brain function.
- Short term outlook (upcoming publications/results)
- Lactobacillus strains alleviated hyperlipidemia and liver steatosis in aging rats via activation of AMPK
- Lactobacillus plantarum DR7 improved brain health in aging rats via the serotonin, inflammatory and apoptosis pathways
- Probiotics from kefir improve gastrointestinal health parameters in adults: A randomised, single-blind, placebo-controlled study
- The molecular mechanism of probiotic strains in promoting healthy aging on the bone and muscle of D-galactose-induced aging rats
- Small intestinal bacteria synergistically play a role in the pathogenesis of experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis
- Commensal bacteria induced by trehalose ameliorates type 1 diabetes mellitus by promoting CD8+ regulatory T cells

Future direction of joint research

- Investigate the potential of probiotics in human vagina health and respiratory illness in children

Student training and fostering of future academic leaders

- Ong Jia Sin, PhD candidate, School of Industrial Technology
- Lye Huey Shi, PhD candidate, School of Industrial Technology
- Hor Yan Yan, PhD graduate, School of Industrial Technology
- Lew Lee Ching, PhD graduate, School of Industrial Technology
- Mohd. Hafis Jaafar, Masters graduate, School of Industrial Technology
- Ahmad Imran Zaydi, Research Officer

Scientific results

Published and accepted manuscripts in refereed journals

- Lye HS, Kato T, Low WY, Taylor TD, Prakash T, Lew LC, Ohno H, Liong MT. 2017. Lactobacillus fermentum FTDC 8312 combats hypercholesterolemia via alteration of gut microbiota. Journal of Biotechnology.

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- Ong JS, Taylor TD, Wong CB, Khoo BY, Sasidharan, Choi SB, Ohno H, Liong MT. 2019 Extracellular transglycosylase and glyceraldehyde-3-phosphate dehydrogenase attributed to the anti-staphylococcal activity of Lactobacillus plantarum USM8613. Journal of Biotechnology
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Oral presentations

- Probiotics for Healthy Aging. Tianjn Science and Technology University Conference on Nutrition and Probiotics. 3-4 June 2019. Tianjin, China
- Lactobacillus plantarum DR7 and the Brain: From Fruit Flies to Human. International Scientific Conference on Probiotics, Prebiotics, Gut Microbiota and Health. 17-20 June 2019. Prague, Czech Republic.
- Lactobacillus and the Aging Brain. 10th Asian Conference on Lactic Acid Bacteria. 28-31 Aug 2019. Yogyakarta, Indonesia
- Relationship of gut microbiota with host diseases. The 45th Japan Society for Bioscience, Biotechnology and Agrochemistry 'Chemistry and Biology' Symposium, March 2019. Tokyo, Japan.
- Gut microbiota in pathogenesis of human diseases. 5th Annual Meeting of the Japanese Society of Nursing and Human Nutrition, March 2019. Tokyo, Japan.
- Impact of small intestinal bacteria on the pathogenesis of experimental autoimmune encephalomyelitis, an animal model of multiple sclerosis. Symposium 15 Role of Gut Microbiota in Health and Disease, KSBMB (Korean Society for Biochemistry and Molecular Biology) International Conference 2019, June 2019. Jeju, Korea.
- Impact of intestinal bacteria on the pathogenesis of autoimmune diseases. International Scientific Conference on Probiotics, Prebiotics, Gut Microbiota and Health. 17-20 June 2019. Prague, Czech Republic.
- Gut microbiota and autoimmune diseases. OIST Workshop “A World of Microbiota” July 2019. Okinawa, Japan.

- Gut microbiota and autoimmune diseases. Azabu University International Symposium on Biological Environment and Human Health Based on Animal Symbiosis Science. July, 2019. Tokyo, Japan.
- Integrated Omics Approach for Understanding the Gut Ecosystem and Autoimmune Disorders. Microbiome Movement, Drug Development & Nutrition Asia Summit. Sept, 2019. Singapore.
- Impact of Gut microbiota on autoimmune diseases. Beneficial Microbes. Sept 2019. Toronto, Canada.
- Gut microbiota and autoimmune diseases. Symposium 28 Microbiome and Immune System 1, IUIS 2019 BEIJING, 17th International Congress of Immunology. Oct. 2019, Beijing, China.
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Catalogue of USM-RIKEN Natural Product (CURINaP) Library for the Discovery of Bioactive Molecules on Ageing and Ageing Related Diseases

Team leaders

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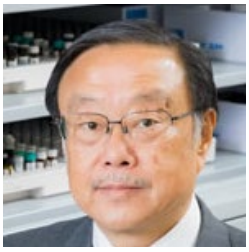

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Team members

- Prof. Dr Kam Zhang (RIKEN, Laboratory of Structural Bioinformatics)
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- Assoc. Prof. Vikneshwaran Murugaiyah (USM)
- Mira Syahfriena Amir Rawa; PhD student; IPA; 3 years dispatched to RIKEN
- Kesevan Rajah Kumaran; PhD student; Post-IPA; 6 months dispatched to RIKEN
- Erma Fatiha Muhammad; PhD student; IPA; 3 years dispatched to RIKEN
- Selestin A/P Rathnasamy; PhD student
- Maram Al Hawari: PhD student
- Nurul Amira Nurul Azman; Master student
- Vincent Ho Yueng Hsing; graduated Master student

Scientific background

The ageing process involved complicated interactions between genetic and environmental factors. Although it in itself, is not regarded as a disease, ageing is linked to many disease conditions, such as cardiovascular, metabolic disorders, neurodegenerative, autoimmune diseases, as well as cancer. Alzheimer disease (AD) is a neurodegenerative disorder mostly affecting elderly people (≥65 years old). Common treatment of AD currently focuses on increasing the level of acetylcholine (ACh) neurotransmitter based on the cholinergic hypothesis approach. To date, there are acetylcholinesterase enzyme inhibitors (AChEIs) approved by the US FDA; that include galanthamine, donepezil, and rivastigmine, in addition to plant based natural products (NP) physostigmine and huperzine A. Encouraged by this discovery of NP AChEIs, we are interested to explore Malaysia's Biodiversity in the search for AChEIs by leveraging the expertise of our RIKEN' collaborator in NP isolations and chemical biology.

There is a pathophysiological link between Alzheimer's Disease, obesity and diabetes mellitus, whereby the CNS insulin resistance plays a significant role as a common mechanism. Metabolic insulin signal transduction is initiated by the tyrosine phosphorylation of insulin receptor, which will then recruit a series of downstream signaling molecules, starting from insulin receptor substrate (IRS) to glucose transporter type 4 (GLUT4) to transport circulating glucose into the cells in-need. Signal arrest at any point of these events may lead to insulin resistance thus an aggravation of blood glucose level. Leptin resistance, metabolic inflammation and stressed endoplasmic reticulum, which are the characteristics of obesity, also

contribute to insulin resistance. Therefore, in another study, we aim to discover potential natural products for the treatment for these metabolic diseases, specifically by targeting protein tyrosine phosphatase 1B (PTP1B). The involvement of this enzyme in many cellular signaling events, especially, the downregulation of insulin and leptin signaling pathways have led to a new novel approach for diabetes and obesity treatment. PTP1B inhibitors might potentially reverse insulin and leptin resistance and normalize plasma leptin, glucose and insulin. Thus, PTP1B is an attractive target for discovery of anti- diabetes and obesity.

Project aim

To expand USM-RIKEN natural product library and discover active fractions and/or compounds for activities with respect to ageing.

Executive summary of research results

One hundred and forty-four plants extracted and stored in USM-RIKEN Catalogue of Natural Products Library, were screened for AChE inhibition, of which fifty-six extracts, were selected for further work based on RIKEN Chemical Biology Research Group's bioassay-guided fractionation method. This work yielded more than 20 compounds isolated. Most active compounds discovered, have the potent activities (0.5- 2 μ M). In USM, seventeen extracts from five species of Cassia were screened for potential AChE inhibitors. C. timorensis showed the highest inhibition and was subjected to further study that led to 8 compounds isolated. Two plants' extracts showed the ability to reduce the weight of mice by 20-40%. Our collaborative work with RIKEN's Laboratory of Structural Bioinformatics have also led to the development of new workflow for structure-based drug discovery from NP scaffold.

Short term outlook

The research has yielded many important results in particular our collaboration has successfully led to the isolation of compounds either for the first time reported to have AChE activity or discovered the first time in the studied plants.

Future direction of joint research

Plant natural product research is very challenging nowadays as expectation to discover novel compounds are increasing despite the facts that most plants secondary metabolites are structurally related and most of their structures have been solved.

However, we are optimistic that more new compounds could be discovered with this joint collaboration and especially more transfer of knowledge in natural products/chemical biology. Most importantly, we hope the realization of USM-RIKEN natural product library will be fully utilised and benefitted by scientists.

Student training and fostering of future academic leaders

- Mira Syahfriena Amir Rawa; current IPA until March 2020, was exposed to hands-on isolation and structure elucidation using high performance equipment including LC-MS, HPLC, MPLC and NMR, that enabled her to isolate and identify more than 20 compounds during her study. She also has been learning cell culture to expand her research skills and search for active metabolites from microbial broth. Altogether this may foster more academicians with specialized research skills for R&D.
- Kesevan Rajah Kumaran; PhD student; post-IPA, undertook cell culture training and has identified a few active metabolites for cancer therapy
- Erma Fatihah; current IPA until 2021 has been exposed to new workflow in structure-based drug design.

Scientific results

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- Kumaran, K. R., Wahab, H. A., & Hassan, Z. 2021. In vitro anti-cholinesterase activity and in vivo screening of Coccoloba uvifera, Mimusops elengi and Syzygium aqueum extracts on learning and memory function of chronic cerebral hypoperfusion rat. Neuroscience Research Notes.
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Oral presentations

- 'Acetylcholinesterase Inhibitors from Malaysian Plants', International Conference on Ageing 2019, Malaysia
- 'A new peptaibol from the soil fungus Trichoderma sp. RK10-F026 by culture condition- dependent screening', The Annual Meeting of the Japan Society for Bioscience, Biotechnology and Agrochemistry 2021, Japan

Poster presentations

- 'Isolation of Acetylcholinesterase Inhibitors from Malaysian Plants', RIKEN Summer School 2017, Japan
- 'Isolation and Structure Elucidation of Acetylcholinesterase Inhibitors from Malaysian Plant Extracts', RIKEN CSRS Interim Progress Report FY2018, Japan
- 'Isolation of Acetylcholinesterase Inhibitors from Malaysian Syzygium Jambos Leaves Extract', RIKEN Summer School 2018, Japan
- 'Inhibitory Activity and Molecular Docking of Acetylcholinesterase Enzyme: Significant to Alzheimer Disease from Cassia sp.',The 2nd International Conference on Medicinal Chemistry 2017, Indonesia
- 'Cassia species as Potential Acetylcholinesterase Inhibitors', International Conference on Ageing 2019, Malaysia
- 'Acetylcholinesterase Inhibitors from Malaysian Plants', The 66th Annual Meeting of the Japanese Society of Pharmacognosy 2019, Japan
- 'Prenylflavonoids from Macaranga tanarius and Anacardic Acids from Syzygium jambos Inhibit AChE in-vitro and in-silico via PAS/CAS Protein- ligand Interactions', RIKEN Summer School 2019, Japan
- 'Acetylcholinesterase Inhibitors from Malaysian Plants', The 24th Chemical and Biological Scientific Meeting, 2019, Japan

Protein, Metabolite and Lipid Profile in T2DM (Type 2 Diabetic Mellitus) Rat Models Upon High Plant Fat Diet Intake

Team leaders

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Team members

- Assoc Prof. Dr Baharuddin Ibrahim (metabolomics)
- Assoc Prof. Dr Vineswaran Murugaya (animal study)
- Dr Mohd Nazri Ismail (mass spectrometry analysis)
- Dr Yan Fen Lee; Postdoc; Post-IPA; 3 months dispatched to RIKEN
- Xuan Ji Lim; PhD candidate; 6 months dispatched to RIKEN as short-term IPA
- Teh Yin Hui; Master course student

Scientific background

It has long been established that type 2 diabetes mellitus (T2DM) is closely associated with unhealthy lifestyles and aging processes. In the elderly, not only reduced beta cell function and proliferation capacity is observed, but also an increase in insulin resistance in most other tissues, leading to a decrease in lean body mass and an increase in body fat. Insulin resistance is known to have a profound effect on mitochondrial activity, ROS levels as well as protein and lipid biosynthesis.

Project aim

The prevalence of T2DM in the population has fuelled a large number of scientific studies in the past. In this project we focus on the early stages of disease onset to identify novel protein markers. Additionally, we focus on the correlation between proteome and changes in the lipidome, highlighting lipid biosynthesis and homeostasis. We specifically focus on sterols and sphingolipids due to their association with arteriosclerosis, neuropathic pain, vitamin D deficiency and cognitive abilities in the elderly.

Executive summary of research results

An animal study with a total of 7 different treatment regimes, including high plant fat treatment, has been jointly planned. After receiving ethical approval, the treatment regime was executed at USM including regular collection of blood and urine samples. In the meantime, RIKEN and USM labs updated and optimized proteome and lipid analysis techniques.

After completion of the animal treatment regime, organs that are expected to be affected by diabetes as well as control tissue were recovered, including kidney, pancreas, brain, liver and smooth muscles. These animal samples were shared between the involved groups. To-date urine metabolome analysis has been completed at USM, while proteomics and lipidome analyses are ongoing. Comparison of protein profiles of

controlled and diseased animals was carried out. Proteins exhibiting a 2-fold differential expression change between two treatment groups were selected and are currently subjected to LC/MS/MS identification.

Lipidome analysis of muscle tissue and brain tissue provided intriguing insights into differences of the sterol homeostasis response. Targeted sphingolipid analysis revealed that increased blood levels of deoxysphingolipids, a specific sphingolipid class associated with neuropathic pain, were not mirrored in brain tissue. Accumulation of steryl hexoside in T2DM brain tissue suggests inhibition of glucosylcerebrosidase (GBA) associated with lysosomal dysregulation.

Short term outlook

Initial results of the animal study and metabolomics analysis have already been reported. Urinary protein markers had been identified. Lipid analysis proofed the presence of elevated levels of a specific neurotoxic sphingolipid class in brain tissue and was correlated with blood values, report in preparation.

Future direction of joint research

Our joint findings highlighted alterations in the brain sterol and sphingolipid biosynthesis during early stage T2DM and the influence of high plant fat diet on lipid homeostasis. Building on these results we are planning to focus on the proteome and lipidome of brain tissue specifically. Key interests are lysosomal dysregulation and its effect on lipid metabolism and protein regulation.

Student training and fostering of future academic leaders

- Dr Yan Fen Lee, after completing her PhD thesis under the RIKEN-IPA programme was selected as URICAS Postdoc to foster her future career at USM and to gain experience in proteomics research.
- PhD - Xuan Yi Sim, was dispatched to RIKEN for 6 months to gain hands on experience in lipid research.
- MSc. - Ying Hui Teh

Scientific results

Published and accepted manuscripts in refereed journals

- Ying-Hui Teh, Xuan-Yi Sim, Yan-Fen Lee, Waqas Ahmad, Vikneswaran Murugaiyah, Baharudin Ibrahim, Mohd Nazri Ismail, Peter Greimel, Lay-Harn Gam. 2019. Urinary Protein Profile Changes in Diabetic Rats and Pre-diabetic Rats Fed with High Fat Diets. Biomedical Research and Therapy.
- Ying-Hui Teh, Xuan-Yi Sim, Yan-Fen Lee, Waqas Ahmad, Vikneswaran Murugaiyah, Baharudin Ibrahim, Mohd Nazri Ismail, Peter Greimel, Lay-Harn Gam. 2020. Potential Urinary Disease Marker for Diabetes. Biomedical Journal of Scientific and Technical Research.
- Yan-Fen Lee, Xuan-Yi Sim, Ying-Hui Teh, Mohd Nazri Ismail, Peter Greimel, Vikneswaran Murugaiyah, Baharudin Ibrahim, Lay-Harn Gam. 2020. The effects of high-fat diet and metformin on urinary metabolites in diabetes and prediabetes rat models. Biotechnology and Applied Biochemistry.
- Xuan-Yi Sim, Waqas Ahmad, Yan-Fen Lee, Ying-Hui Teh, Vikneswaran Murugaiyah, Baharudin Ibrahim, Peter Greimel, Lay-Harn Gam. 2020. Weight Gain and Adipose Tissue Accumulation in Diabetic and Prediabetic Rats Fed with Palm Olein enriched High Fat Diet. Journal of Biochemistry, Microbiology and Biotechnology.
- Sim Xuan-Yi, Baharudin Ibrahim, and Lay-Harn Gam. 2021. Urinary metabolites of type 2 diabetes rats fed with palm oil-enriched high fat diet. Heliyon.
- Lee Yan Fen, Gam Lay Harn, Sim X.Yi, Mohd Nazri Bin Ismail. 2021. Overexpression of Hsc 70 and pyruvate dehydrogenase in the brain tissue at the early stage of high fat diet consumption. HAYATI Journal of Biosciences.

Oral presentations

- "The effect of high fat diet intake on blood glucose level of prediabetic and type 2 diabetic rats"; Xuan Yi Sim, Baharudin Ibrahim, Vikneswaran Murugaiyah, Peter Greimel, Lay Harn Gam; MPS-USM Pharmacy Scientific Conference; Bayview Beach Hotel, Penang 2017
- "Ageing, Diabetes Melitus and Sphingolipid Metabolism"; S. Kargoll, XY Sim, YF. Lee, V. Murugaiyah, LH Gam, P. Greimel; International Conference on Ageing (ICA), Penang, 2019

Poster presentations

- "Adipose Tissue Accumulation In Diabetic and Prediabetic Rats Fed With Normal and High Fat Diets"; Xuan-Yi Sim, Waqas Ahmad, Yan-Fen Lee, Ying-Hui Teh, Vikneswaran Murugaiyah, Baharudin Ibrahim, Peter Greimel, Lay-Harn Gam; International Conference on Ageing (ICA), Penang, 2019.
- "Urinary Protein Profile Changes in Diabetic Rats and Pre-diabetic Rats Fed with High Fat Diets"; Ying-Hui Teh, Xuan-Yi Sim, Yan-Fen Lee, Waqas Ahmad, Vikneswaran Murugaiyah, Baharudin Ibrahim, Mohd Nazri Ismail, Peter Greimel, and Lay-Harn Gam ; International Conference on ageing 2019.
- "The effect of metformin on urinary metabolomic profile of diabetic and prediabetic rats upon high fat diet intake"; Xuan Yi Sim, Peter Greimel, Baharudin Ibrahim, Vikneswaran Murugaiyah, Lay Harn Gam; USM-RIKEN International Center for Aging Science (URICAS), 2017.

Development of New Biopolymers for Medical and Therapeutic Applications in Aged Patients

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- Dr Chuah Jo-Ann
- Dr Manoj Kumar Lakshmanan; Post-doctoral Research Fellow; Post-IPA; 6 months attachment at RIKEN
- Ms Ang Shaik Ling; Master student
- Ms Iffa Farahin (PhD student - IPA student attached at RIKEN)

Scientific background

Advanced age results in various complications during surgery and interventional therapy. The main causes of which can be attributed to the slow healing process in aged patients and the choice of biomaterials used. In the current clinical setting, there are only limited number of polymeric biomaterials being utilised, and stiff synthetic patches are unable to adequately heal repaired tissues. In this project, polyhydroxyalkanoate (PHA) and silk fibroin (SF) are being studied to develop a new polymeric biomaterial that is for medical and therapeutic applications in aged patients.

Project aim

To develop new biopolymers that have a wide range of properties and functions suitable for aged patients and slow healing interventional treatments.

Executive summary of research results

The proliferation and osteogenic differentiation of human mesenchymal stem cells (hMSCs) were enhanced through the blending of PHA and SF. The hMSCs expressed higher osteogenic marker genes when cultured on electrospun PHA/SF film compared to electrospun PHA and electrospun SF films. This suggests that electrospun PHA/SF film is a promising biomaterial for bone regeneration for osteoporotic elderly patients.

Short term outlook

A novel PHA synthase gene has been identified from a mangrove metagenome. This newly identified PHA synthase showed the ability to polymerise various types of PHA monomers, for instance, 4-hydroxybutyrate and 5-hydroxyvalerate which can be degraded by lipases which is essential for bioresorbable materials. We

expect this novel PHA synthase will be able to synthesize new biomaterials that are suitable for designing better implantable scaffolds.

Future direction of joint research

Based on the current results, our future direction will be focusing on developing tissue engineering scaffold using 3D printing technology. The fabricated scaffolds will be targeting aged patients who have osteoporosis. Besides, in vitro bone disease models will be created to understand the disease pathology and drug screening.

Student training and fostering of future academic leaders

- Dr Manoj Kumar Lakshmanan
- Ms Ang Shaik Ling
- Ms Iffa Farahin

Scientific results

Published and accepted manuscripts in refereed journals

- The Influence of Electrospinning Parameters and Drug Loading on Polyhydroxyalkanoate (PHA) Nanofibers for Drug Delivery, Yan-Fen Lee, Nanthini Sridewi, Surash Ramanathan and Kumar Sudesh, International Journal of Biotechnology for Wellness Industries (2015).
- Green Nanotechnology for Synthesis and characterization of poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) nanoparticles for sustained bortezomib release using supercritical CO2 assisted particle formation combined with electrodeposition, Demirdöğen, Ruken Esra, Fatih Mehmet Emen, Kasim Ocakoglu, Paramasivam Murugan, Kumar Sudesh, and Göktürk Avşar. International Journal of Biological Macromolecules (2018).
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- Biosynthesis and Characterization of Co- and Ter-Polyesters of Polyhydroxyalkanoates Containing High Monomeric Fractions of 4- Hydroxybutyrate and 5-Hydroxyvalerate Via a Novel PHA Synthase, Manoj Lakshmanan, Choon Pin Foong, Hideki Abe and Kumar Sudesh, Polymer Degradation and Stability (2019).
- High cell density culture of Cupriavidus necator H16 and improved biological recovery of polyhydroxyalkanoates using mealworms. Idris Zainab-L, Sudesh, K. Journal of Biotechnology (2019).
- Electrospun poly(3-hydroxybutyrate-co-3-hydroxyhexanoate)/silk fibroin film is a promising scaffold for bone tissue engineering. Shaik Ling Ang, Bakiah Shaharuddin, Jo-Ann Chuah, Kumar Sudesh. International Journal of Biological Macromolecules (2019).
- Complete Genome Sequence of a Novel Polyhydroxyalkanoate (PHA) Producer, Jeongeupia sp. USM3 (JCM 19920) and Characterization of Its PHA Synthases. Noor-Afiqah Ahmad Zain, Lee-Mei Ng, Choon Pin Foong, Yen Teng Tai, Jayaram Nanthini, Kumar Sudesh. Current Microbiology (2020).
- Potential Applications of Polyhydroxyalkanoates as a Biomaterial for the Aging Population. Shaik Ling Ang, Ramamoorthi Sivashankari, Bakiah Shaharuddin, Jo-Ann Chuah, Takeharu Tsuge, Hideki Abe, Kumar Sudesh. Polymer Degradation and Stability (2020).
- Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome. Pulingam, Thiruchelvi, Thaigarajan Parumasivam, Amirah Mohd Gazzali, Azlinah Mohd Sulaiman, Jiun Yee Chee, Manoj Lakshmanan, Chai Fung Chin, and Kumar Sudesh. European Journal of Pharmaceutical Sciences (2021)

Oral presentations

- 'Biosynthesis and Characterization of Co and Ter-Polyesters of Polyhydroxyalkanoates Containing High Monomeric Fractions of 4- Hydroxybutyrate and 5-Hydroxyvalerate Via a Novel PHA Synthase', International Symposium on Science and Technology (ISST), 2017, Kompleks Cahaya, USM.
- 'Biocompatibility and Osteogenic Differentiation Potential of Primary Human Mesenchymal Umbilical Cord Stem cells on Novel Polyhydroxyalkanoate (PHA) Scaffolds,' Bioplastic Global Joint Symposium, 2019, University of The Philippines, Mindanao.

Poster presentations

- 'A Novel Wide Substrate Specificity Polyhydroxyalkanaote (PHA) Synthase from Uncultured Mangrove Bacterium', International Conference of Bio-based Polymers (ICBP), 2017, Yuan Ze University, Taiwan
- 'Fabrication of Biomaterial Scaffold Using Bombyx mori Silk Fibroin with Poly(3-hydroxybutyrate-co-3-hydroxyhexanoate)', URICAS Symposium, 2017, Institute for Research in Molecular Medicine (INFORMM), USM.
- 'Biosynthesis of Co-Polyesters of Polyhydroxyalkanoates Containing High Monomeric Fractions of 4-Hydroxybutyrate and 5-Hydroxyvalerate Via a Novel PHA Synthase', The 10th International Conference of Modification, Degradation and Stabilization of Polymers 2018, The University of Tokyo, Japan.
- 'In vitro Biocompatibility Study of Electrospun Poly(3-hydroxybutyrate-co-3- hydroxyhexanoate)/Silk Fibroin as Biomaterial Scaffold Towards Bone Tissue Engineering Application', URICAS Symposium 2019, Institute for Research in Molecular Medicine (INFORMM).
- 'Electrospun Poly(3-hydroxybutyrate-co-3-hydroxyhexanoate)/Silk Fibroin Is A Promising Scaffold For Bone Tissue Engineering', 7th International Conference on Bio-based Polymers (ICBP 2019), Bangkok, Thailand
- 'Biosynthesis and Characterization of Polyhydroxyalkanoates Potential for Various Biomedical Applications in Aged Patients', International Conference on Ageing, 2019, Eastin Hotel Penang.

Patents

- Production of polyhydroxyalkanoic acid by only photosynthesis, Matsui Minami, Kurihara Yukio, Lau Nyok Sean, Foong Choon Pin, Kumar Sudesh, 2019, Patent number: 6492011
- Composition for suppressing function of Cryptochrome, Minami Matsui, Yukio Kurihara, Emiko Kurihara, WenDee Ong, Kumar Sudesh, 2016, Application number:2016-205506

The Anti-senescence Effects of Mesenchymal Stem Cells (MSC)-Derived Extracellular Vesicles (Evs) on COPD

Team leaders

Assoc. Prof. Dr Badrul Hisham Yahaya
Universiti Sains Malaysia
Advanced Medical and Dental Institute

Dr Mitsuru Morimoto
RIKEN
Center for Biosystems Dynamics Research

Team members

- Norashikin Zakaria (USM)
- Ridzzaida Redzuan (USM)
- Takashi Fujimura (RIKEN)
- Hirofumi Kiyokawa (RIKEN)

Scientific background

Dr Morimoto's lab of RIKEN BDR focuses on investigating fundamental principles conserved in development and regeneration of the respiratory organs and their roles in human disease. Morimoto's lab has knowledge and technologies in mouse genetic analysis, high-resolution 4D imaging for fetal tissue, in vitro reconstruction of respiratory tissue from stem cells which is known as "Organoids". He and his group has discovered that Notch signaling regulates 6 different lung cell types during development (Morimoto et al., J. Cell. Sci. 2010, Development 2012, Noguchi et al., Cell Reports 2015, Tsao et al., PNAS 2016), also found that tracheal tube morphogenesis is regulated by synchronized mesenchymal cell polarity via Wnt5a signaling (Kishimoto et al., Nature Communications 2018).

Dr Yahaya's lab focuses on a basic understanding on pathophysiological and molecular changes of the airway during injury and repair. To achieve that, animal models were developed for both chronic and acute lung injuries using various model system that include sheep, rabbit, rat and mice. Dr Yahaya's lab has also developed technology for cell therapy as one of the approaches to facilitate airway regeneration and repair. His group has innovated an aerosol-based cell delivery as a technique for delivering cells into lungs to treat acute and chronic lung diseases that can eliminate the conventional technique for cell therapy using intravenous (iv) injection. His group currently has established a cell-free therapy approach as an alternative treatment for chronic lung diseases (i.e. preclinical study for asthma and COPD) using extracellular vesicles derived from mesenchymal stem cells (MSC). Besides, Dr Yahaya's lab is interested to understand the roles of stem cells in lung development and lung injury using lung organoid model system. This might be the key towards identification of specific target cells to treat airway diseases.

Project aim

The lung is the organ which taking external air with various stimulant factors such as virus, germs as well as toxic chemical particles. These external stimulants frequently caused damage to the airways and alveolar tissues that lead to defect in breathing if the damaged in severe. Since both Dr Yahaya's and Dr Morimoto's

lab are interested in tissue repair of lung especially on the potential use of tissue stem cells, collaborative project was initiated with funding given by both parties. The project focuses on the effect of mesenchymal stem cells and its secretion compounds on airway tissue regeneration and repair following smoking-induced COPD with the aim to understand the cellular and molecular mechanisms of lung repair mediated by stem cells. As our interest to use both lung development concept and preclinical disease modelling system to study the roles of stem cells in lung development and repair with the hope to identify specific target cells to treat lung diseases and contributes to developing the next generation regenerative medicine for respiratory diseases.

Executive summary of research results

In order to find a topic for collaboration, we started to exchange people and technologies each other. Dr Yahaya visited RIKEN Kobe 2 times where at first visit was initiative for research collaboration whilst the second was to learn on lung organoid culture. Dr Morimoto was invited as a speaker during 6th Malaysian Tissue Engineering and Regenerative Medicine (MTERM) Meeting in 2016 organized by Tissue Engineering and Regenerative Medicine Society of Malaysia (TESMA) where Dr Yahaya was the chairman of the organizing committee. For technology exchange programme, Dr Yahaya and his postdoc Dr Norashikin learnt a 3D-lung stem cell culture protocol, called alveolar organoid culture, which can create "mini-alveoli" on dish during their visit. With the funding supported by grants from Dr Yahaya and Dr Morimoto, Dr Norashikin was attached to Dr Morimoto's lab for a week to run experiment on transcriptome analysis using DNA microarray in the Dr Morimoto's lab, in which this project is part of the output from Dr Yahaya's USM-funded grant where Dr Morimoto is one of the co-investigators. Dr Yahaya is using these technologies to advance his research in lung regeneration from the emphysema in rat.

Short term outlook

Dr Yahaya's group is still establishing organoid culture using methods established by Dr Morimoto's lab. However, Dr Yahaya's group is still not be able to establish it due to various challenges. Recently, Dr Yahaya group has received funding from Ministry of Education Malaysia via Fundamental Research Grant Scheme (FRGS) to study on the effect of smoking-induced COPD on stemness capability of lung stem cells in tissue repair, and this 3-year project is continuation from the collaborative project with Dr Morimoto's lab. Dr Yahaya will study further on the lung organoid culture and this will be the 2nd-phase of their collaboration with Dr Morimoto's lab.

In terms of the current collaborative study with Dr Morimoto's lab on the effect of MSC on lung repair, where the microarray experiment was conducted in Dr Morimoto's lab, Dr Yahaya's team is still analysing the data and preparing manuscript for high impact publication. Basically, there were four groups of animals were studied i.e., Naïve (healthy animal), cigarette smoke (CS as an injury group), cigarette smoke treated with MSC-derived extracellular vesicles (CSEV), and cigarette smoke treated with MSC (CSMSC) and were subjected to microarray analysis. Analysis were conducted using GeneSpring software. There were 161 pathways observed in CS vs Naïve, EV vs CS, and MSC vs CS group, 157 pathways were observed in CSEV vs CSMSC, 91 pathways were observed in CSEV vs Naïve, and 134 pathways were observed in CSMSC vs Naïve. Inflammatory pathways, as well as apoptosis, and senescence pathways and many pathways related to metabolic and lung development were observed in the study. Upregulation of inflammation, apoptosis, and senescence related genes were significantly observed in CS group. However, treatment with MSC- EV, and MSC were significantly downregulated many of these genes. Understanding the roles of inflammatory and anti-inflammatory related genes in regulating airway repair in smoking-induced COPD model system might lead to identification of specific genes and pathways for treatment of COPD thus could be further understand their roles in lung development.

Future direction of joint research

We will cooperate in the project "Regenerative potential of lung stem cells in COPD model" in which we will develop protocols to measure the stemness of alveolar tissue of COPD-model mice using 3D-lung stem cell culture method, also explore factors improving proliferation of the stem cells in vitro and tissue repair in vivo.

Student training and fostering of future academic leaders

Postdocs in Dr Morimoto's lab organized the technology exchange of 3D-lung stem cell culture protocol and DNA microarray analysis. Dr Yahaya's postdoc, Dr Norashikin was stayed at Kobe for a week not only for learning technologies but also to know research styles of researched in RIKEN and the culture in science in Japan. Dr Yahaya's group will provide technology for the development of disease modelling which might involve smoking-induced for chronic lung disease or acute lung injury, whichever applicable to the study objective. Dr Yahaya's group also will provide technology related to stem cell delivery or therapy and relates those model systems with lung development study (cell lineage and tracking) by Dr Morimoto.

Scientific results

Published and accepted manuscripts in refereed journals

- Conditioned Medium of Human Menstrual Blood-Derived Endometrial Stem Cells Protects Against MPP+-Induced Neurotoxicity In Vitro. Han Li, Badrul Hisham Yahaya, Wai Hoe Ng, Narazah Mohd Yusoff and Juntang Lin. 2019. Frontiers in molecular neuroscience.
- Human Umbilical Cord Mesenchymal Stem Cell Derived Extracellular Vesicles Ameliorate Airway Inflammation in a Rat Model of chronic obstructive pulmonary disease (COPD). Noridzzaida Ridzuan, Norashikin Zakaria, Darius Widera, Jonathan Sheard, Mitsuru Morimoto, Hirofumi Kiyokawa, Seoparjoo Azmel Mohd Isa, Gurjeet Kaur Chatar Singh, Kong-Yong Then, Ghee-Chien Ooi, Badrul Hisham Yahaya. 2021. Stem Cell Research and Therapy.
- Acute Lung Injury: Disease Modelling and the Therapeutic Potential of Stem Cells. Jie Lian, Juntang Lin, Norashikin Zakaria, Badrul Hisham Yahaya. 2020. Advances in Experimental Medicine and Biology.
- Synergistic Roles of Curcumin in Sensitising the Cisplatin Effect on a Cancer Stem Cell-Like Population Derived from Non-Small Cell Lung Cancer Cell Lines. Nazilah Abdul Satar, Mohd Nazri Ismail and Badrul Hisham Yahaya. 2021. Molecules.

Published Book Chapters

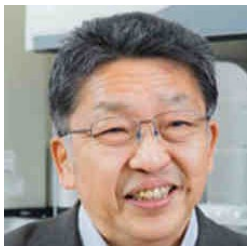
- Secretome of Mesenchymal Stem Cells and its Impact on Chronic Obstructive Pulmonary Disease. Noridzzaida Ridzuan, Darius Widera, Badrul Hisham Yahaya. 2019. Stem Cell Transplantation for Autoimmune Diseases and Inflammation.
- Adipose-derived mesenchymal stem cells promote growth and migration of lung adenocarcinoma cancer cells. N Zakaria, BH Yahaya. 2020. Cancer Biology and Advances in Treatment.
- Acute Lung Injury: Disease Modelling and the Therapeutic Potential of Stem Cells. Jie Lian, Juntang Lin, Norashikin Zakaria, Badrul Hisham Yahaya. 2020. Advances in Experimental Medicine and Biology.

Synthetic Compounds Screening for Alzheimer's Disease using Drosophila melanogaster

Team leaders

Prof. Dr Nazalan Najimudin
Universiti Sains Malaysia
School of Biological Sciences

Assoc. Prof. Dr Ghows Azzam
Universiti Sains Malaysia
School of Biological Sciences



Dr Nobumoto Watanabe
RIKEN
Center for Sustainable Resource Science

Team members

- Florence Tan; PhD student; Post-IPA; 5 months dispatched to RIKEN
- Dr Mardani Halim; Postdoc (joint with Prof. Shaharum Shamsuddin)
- Leow Ban Guan; Final Year Project student
- Ng Jia Chen; Final Year Project student
- Nurulhuda Athirah binti Hadri; Final Year Project student
- Go Wen Chen; Final Year Project student

Scientific background

Alzheimer's disease (AD) is the most common form of neurodegenerative disorder worldwide. Its pathogenesis involves the hallmark aggregation of amyloid-beta (Aβ). Of all the Aβ oligomers formed in the brain, Aβ42 has been found to be the most toxic and aggressive. Despite this, the mechanism behind this disease remains elusive with no cure in sight. Drosophila melanogaster with the ability to utilize various genetic manipulations, is ideal in analysing not only cellular characteristics but also physiological and behavioural traits of human neurodegenerative diseases. To understand the underlying pathogenesis of AD, transgenic fly models that undertake amyloid toxicity caused by the hallmark amyloid-beta 42 (Aβ42) protein have been developed and screening of compounds from was conducted.

Project aim

To discover novel neuroprotective compounds that can ameliorate Aβ42's effects.

Executive summary of research results

To identify potential compounds, a chemical array assay was utilized to screen 22,097 compounds from RIKEN's NPDepo library wherein a total of 165 compounds were discovered to be Aβ42 ligands. From these ligands, 16 compounds were found to be potential inhibitors of Aβ42 aggregation based on an in vitro activity assay. As Aβ42 causes neurodegeneration to neurons, these potential inhibitors were tested on Aβ42- incubated PC12 neuronal cells in which 15 compounds showed increased cell viability.

These hit compounds were then tested on the Drosophila AD model and their rescue effects were characterized. From here, eight compounds were found to diminish Aβ42's defects on Drosophila melanogaster. Through screening using three different Drosophila assays, few compounds were able to reverse Aβ42's effects on neurodegeneration and lifespan.

Short term outlook

- The neuroprotective effect of Danshen on Drosophila melanogaster's Alzheimer model. Manuscript in preparation
- Novel synthetic compounds with neuroprotective effect on Drosophila melanogaster. Patent and manuscript in preparation
- Microbiome changes of Alzheimer's Drosophila model treated with synthetic compounds. On-going work
- Transcriptome analysis reveals specific pathway changes in Drosophila
- Alzheimer model.

Future direction of joint research

There are still many compounds that have not been tested in the lab. Furthermore, new novel synthetic compounds are currently being developed in RIKEN. The RIKEN compounds can also be tested for tumour phenotype that is currently being studied in the USM lab.

Student training and fostering of future academic leaders

- Florence Tan; PhD student; Post-IPA; 3 months dispatched to RIKEN undertaking hands-on training on the screening of compounds and how compounds are synthesized. Furthermore, she was also taught on how to work with PC12 neuronal cells.
- Dr Mardani Halim; Postdoc (joint with Prof. Shaharum Shamsuddin). Dr Mardani is undertaking cross disciplinary research together with Dr Kuniya Abe (RIKEN BioResource Research Center) to study epigenetics, and Dr Isao Watanabe (Meson Science Laboratory) to study the use of Muons on nucleic acids. These new projects are high impact projects with both short- and long-term goals.
- Leow Ban Guan and Ng Jia Chen undertook their Final Year Project student in USM based on the Alzheimer's disease project.

Scientific results

Published and accepted manuscripts in refereed journals

- Drosophila melanogaster – Deciphering Alzheimer's disease. Tan F. and Azzam G. (2017). Malays J Med Sci. 2017;24(2):6–20. doi: 10.21315/mjms2017.24.2.2
- Genome-wide identification and characterization of long intergenic noncoding RNAs in the regenerative flatworm Macrostomum lignano. Azlan A., Halim M.A. and Azzam G. (2019). Genomics. DOI: 10.1016/j.ygeno.2019.07.016
- Lactobacillus plantarum DR7 improved brain health in aging rats via the serotonin, inflammatory and apoptosis pathways. A.I. Zaydi, L.-C. Lew, Y.-Y. Hor, M.H. Jaafar, L.-O. Chuah, K.-P. Yap, A. Azlan, G. Azzam, M.-T. Liong. 2020. Beneficial Microbes.
- Lactic acid bacteria feeding reversed the malformed eye structures and ameliorated gut microbiota profiles of Drosophila melanogaster Alzheimer's Disease model. Guoxia LIU, Florence Hui-Ping TAN, Sie-Yik Amy LAU, Mohamad Hafis JAAFAR, Fiona Yi-Li CHUNG, Ghows AZZAM, Min-Tze LIONG, Yin LI. 2020. Journal of Applied Microbiology.
- Ageing, Drosophila melanogaster and Epigenetics. Mardani Abdul Halim, Florence Hui Ping Tan, Azali Azlan, Ian Ilham Rasyid, Nurlina Rosli, Shaharum Shamsuddin, Ghows Azzam. 2020. Malaysian Journal of Medical Sciences.
- Effects of Salvianolic Acid A on Β-Amyloid Mediated Toxicity in Caenorhabditis elegans Model of Alzheimer's Disease. Yuen Chee Wah, Mardani Abdul Halim, Nazalan Najimudin, Ghows Azzam. 2020. Journal of Biomedical and Clinical Sciences.

- Danshen (Salvia miltiorrhiza) water extract shows potential neuroprotective effects in Caenorhabditis elegans. Chee Wah Yuen, Vikneswaran Murugaiyah, Nazalan Najimudin, GhowsAzzam. 2021. Journal of Ethnopharmacology.
- Lactobacillus Strains Alleviated Hyperlipidemia and Liver Steatosis in Aging Rats Via Activation of AMPK. Lee-Ching Lew, Yan-Yan Hor, Mohamad-Hafis Jaafar, Amy-Sie-Yik Lau, Boon-Kiat Lee, Li-Oon Chuah, Kien-Pong Yap, Azali Azlan, Ghows Azzam, Sy-Bing Choi, Min-Tze Liong. 2020. International Journal of Molecular Sciences.
- The molecular mechanisms of probiotic strains in improving ageing bone and muscle of d-galactose-induced ageing rats. Y.-Y. Hor, C.-H. Ooi, L.-C. Lew, M.H. Jaafar, A.S.-Y. Lau, B.-K. Lee, A. Azlan, S.-B. Choi, G. Azzam, M.-T. Liong. 2020. Journal of Applied Microbiology.
- Lactobacillus probiotics improved the gut microbiota profile of a Drosophila melanogaster Alzheimer's disease model and alleviated neurodegeneration in the eye. Tan F.H.P., Liu G., Lau S.-Y.A., Jaafar M.H., Park Y.-H., Azzam G., Li Y., Liong M.-T. 2020. Beneficial Microbes.
- Lactobacilli modulated AMPK activity and prevented telomere shortening in ageing rats. Lew LC, Hor YY, Jaafar MH, Lau ASY, Ong JS, Chuah LC, Yap KP,Ghows A, Azali A, Liong MT. 2019. Beneficial Microbes.
- Lactobacillus sp. improved microbiota and metabolite profiles of aging rats. Hor YY, Lew LC, Jaafar MH, Lau ASY,Ong JS, Kato T, Nakanishi Y, Ghows A, Azali A, Ohno H, Liong MT. 2019. Pharmacological Research.
- Ethyl caffeate ameliorated amyloid-beta42 protein-associated toxicity in PC12 cells and Drosophila melanogaster. Tan, F.H.P., Hadri, N.A.B., Najimudin, N., Watanabe, N. and Azzam, G.. 2021. Geriatrics & gerontology international.
- Alleviatory effects of Danshen, Salvianolic acid A and Salvianolic acid B on PC12 neuronal cells and Drosophila melanogaster model of Alzheimer's disease. Tan, F.H.P., Ting, A.C.J., Leow, B.G., Najimudin, N., Watanabe, N. and Azzam, G.. 2021. Journal of ethnopharmacology.

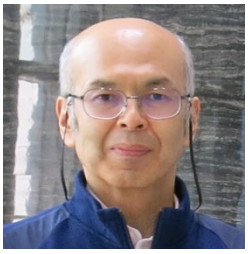
Oral presentations

- Drosophila melanogaster: A Drug Discovery tool for Alzheimer's disease URICAS Symposium 2017
- Screening of neuroprotective compounds against Alzheimer's disease URICAS Symposium 2018
- Compound screening for Alzheimer's disease International Conference on Ageing 2019 (ICA 2019)

Understanding Electron Transport in DNA: μSR and First-Principle Computational Investigations

Team leaders

Prof. Dr Shukri Sulaiman
Universiti Sains Malaysia
School of Distance Education



Dr Isao Watanabe
RIKEN
Meson Science Laboratory

Team members

- Prof. Dr Shukri Sulaiman
- Prof. Dr Isao Watanabe
- Dr Wan Nurfadhilah Zaharim
- Dr Hasni Arsad
- Dr Daruliza Kernain Mohd Azman
- Harison Rozak, PhD/IPA student

Scientific background

Various biological processes in DNA such as storage and consumption of energy, enzyme response, and UV damage repair, are strongly related to electron transfer through DNA. DNA can be damaged by both external (exogenous) and internal metabolic (endogenous) processes. One normal cell metabolism that can cause damage to DNA nitrogenous base is alkylation process. Alkylation modification in the form of methylation results in minor structural changes where methyl groups are added to the nitrogen or oxygen atoms of the bases. Human genome contains approximately 30,000 CpG islands. Methylation of cytosine (C) to 5-methylcytosine (5MeC) is most common at CpG island. The methylation of C is an epigenetic gene regulatory mechanism with implications for ageing and disease. Guanine base can also be methylated to O6- methylguanine (O6MeG), which can lead to cell cycle arrest or apoptosis. The unrepaired O6MeG is a major cause for diseases. Those damages are considered to cause alteration of the electron transfer in DNA. Accordingly, the study of the electron transfer of DNA is an important key factor to investigate the mechanism of those diseases. Presently, the degree and type of alterations of the electron transport due to different damages in DNA are quantitatively unknown at the microscopic level.

Pioneering work by Torikai et al. to study electron transfer in perfect DNA's at the microscopic level using the muon spin relaxation (μSR) method opened up avenues for novel research in this area and provided a new perspective in the understanding of ageing. However, they have used real DNA samples derived from the Herring's sperm. The actual base-pair sequence of the sample they used was complex and unknown. Therefore, it was difficult to make further analysis and studies with respect to damages in DNA based on their findings.

The limitation arises from using real DNA samples to study electron transport can be removed by approaching the research problem differently. In particular, the structural complexity problem must be broken down into smaller problems to build a baseline data. We have developed a framework to approach

this research problem. Our approach in studying the effects of damages to the nature of electron transport in DNA at the atomic level are μSR, Transmission Electron Microscopy (TEM), Scanning Tunnelling Microscope (STM), and UV-visible (UV-Vis) spectrophotometry. The actual atomic arrangement in the molecule (atomic coordinates) and the electronic structure of the molecule are determined using Density Functional Theory (DFT) calculations and Molecular Dynamic Simulations (MDS).

Project aim

The aim of this project is to quantify at microscopic level the effects of damages in DNA to the properties of electron transport.

Executive summary of research results

We have performed μSR measurements using four synthetic single strand DNA (ssDNA) samples. Our conclusion from this measurement is that the electron transfer is distinct in each sample and the dimensionality of the electron motion is quasi- one-dimensional (1D). The observation of clear image indicates that 12mer ssG is electronically conductive. Interestingly, molecules were aligned via the side-by-side connection forming the 1D chain structure.

DFT cluster method was applied to investigate the possible muonium trapping sites in isolated guanine, guanine nucleobase and guanine nucleotide. The addition of muonium to these three systems give a similar effect to the in-plane characteristic of guanine base. The position C8 atom was found to be the lowest one in energy and represents the most likely stable site for muonium. The Fermi contact coupling constant for muonium trapped at C8 atom in isotropic guanine, guanine nucleobase, and guanine nucleotide systems are 337.366 MHz, 332.281 MHz, and 310.584 MHz respectively.

Short term outlook

- Zaharim, W. N., Mohd-Tajudin, S. S., Sulaiman, S., Abu Bakar, S. N., Ismail, N. E., Rozak, H., & Watanabe, I. Simulation and Observation of 12mer Single Strand Guanine Oligomer. Advances in Experimental Medicine and Biology. (accepted) (WOS Indexed)
- Zaharim, W. N., Mohd-Tajudin, S. S., Sulaiman, S., Abu Bakar, S. N., Ismail, N. E., Rozak, H., & Watanabe, I. Density Functional Theory Investigation of Guanine and Cytosine. Advances in Experimental Medicine and Biology. (accepted) (WOS Indexed)
- Rozak, H., Sulaiman, S., Zaharim, W. N., Miyazaki, I., Ismail, N. E., Abu Bakar,
- S. N., Samian, M. R., Ichimura, K., Mohamed-Ibrahim, M. I., & Watanabe, I. Electrical Conductivity Measurements of 1 2-mer Single-Stranded Guanine Molecule in Dry and Humid Condition. Advances in Experimental Medicine and Biology. (accepted) (WOS Indexed)
- Zaharim, W. N., Sulaiman, S., Abu Bakar, S. N., Ismail, N. E., Rozak, H., & Watanabe, I. First Principles Theory of Hyperfine Interactions in Guanine Nucleobase. ICMR 2019 – 8th International Conference on Multidisciplinary Research. (accepted) (WOS Indexed)
- Zaharim, W. N., Mohd-Tajudin, S. S., Sulaiman, S., Abu Bakar, S. N., Ismail, N. E., Rozak, H., & Watanabe, I. Density Functional Theory Studies on Muonium Trapping Sites in 12mer Single Strand Guanine Oligomer. (In preparation)
- Rozak, H., Sulaiman, S., Zaharim, W. N., Miyazaki, I., Ismail, N. E., Abu Bakar,
- S. N., Samian, M. R., Ichimura, K., & Watanabe, I. Electrical Conductivity Measurement of Synthetic Single Strand DNA by Scanning Tunnelling Microscope and Muon Spin Relaxation. (In preparation)
- Density Functional Theory Studies of Muon Stopping Sites and Hyperfine Interaction in [Au25(SR)18]0 Nanocluster. Journal of the Physical Society of Japan. (accepted) (WOS indexed)

Future direction of joint research

We have completed our investigation using single strand DNA samples. We will continue the project to study the normal and methylated double strand DNA samples. We are applying for the Newton Fund research grant to continue the project.

Student training and fostering of future academic leaders

- PhD student: graduated (Dr Wan Nurfadhilah Zaharim)
- PhD/IPA student: finishing (Mrs. Noraina Adam)
- PhD/IPA student: finishing (Ms Saidah Sakinah Mohd-Tajudin)
- PhD/IPA student: finishing (Ms Harison Rozak)

Scientific results

Published and accepted manuscripts in refereed journals (URICAS related)

- Zaharim, Wan Nurfadhilah, Harison Rozak, Shukri Sulaiman, Siti Nur Afifi Ahmad, Dang Fatihah Hasan Baseri, Saidah Sakinah Mohd-Tajudin, Ang Lee Sin, and Isao Watanabe. "Density Functional Theory Investigation of Hyperfine Interaction in DNA Nucleobase and Nucleotide Muoniated Radicals." Journal of the Physical Society of Japan, vol. 90, no. 4 (2021).
- Zaharim, Wan N., Siti NA Ahmad, Shukri Sulaiman, Harison Rozak, Dang F. Hasan Baseri, Nur A. Mohamad Rosli, Saidah S. Mohd-Tajudin, Lee S. Ang, and Isao Watanabe. "Density Functional Theory Study of 12mer Single-Strand Guanine Oligomer and Associated Muon Hyperfine Interaction." ACS omega, vol. 6, no. 44 (2021).
- Ramli, Irwan, Saidah Sakinah Mohd Tajudin, Muhammad Redo Ramadhan, Dita Puspita Sari, Shukri Sulaiman, Mohamed Ismail Mohamed-Ibrahim, Budhy Kurniawan, and Isao Watanabe. "Magnetic properties of YBa2Cu3O6 studied by density functional theory calculations." In Materials Science Forum, vol. 966, pp. 257-262. Trans Tech Publications Ltd (2019).
- Angel, Julia, Retno Asih, Hironori Nomura, Tomoya Taniguchi, Kazuyuki Matsuhira, Muhammad Redo Ramadhan, Irwan Ramli et al. "Magnetic Properties of Hole-Doped Pyrochlore Iridate (Y1-x-yCuxCay)2Ir2O7." In Materials Science Forum, vol. 966, pp. 269-276. Trans Tech Publications Ltd (2019).
- Ramadhan, Muhammad Redo, Irwan Ramli, Muhamad Darwis Umar, Suci Winarsih, Dita Puspita Sari, Azwar Manaf, Budhy Kurniawan, Mohamed Ismail Mohamed-Ibrahim, Shukri Sulaiman, and Isao Watanabe. "Effects of the supercell's size on muon positions calculations of La2CuO4." In Materials Science Forum, vol. 966, pp. 465-470. Trans Tech Publications Ltd (2019).
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- Zaharim, Wan Nurfadhilah, Shukri Sulaiman, Siti Nuramira Abu Bakar, Nur Eliana Ismail, Harison Rozak, and Isao Watanabe. "The effects of split valence basis sets on muon hyperfine interaction in guanine nucleobase and nucleotide structures." In Materials Science Forum, vol. 966, pp. 222-228. Trans Tech Publications Ltd (2019).
- Rozak, Harison, Wan Nurfadhilah Zaharim, Issei Miyazaki, Nur Eliana Ismail, Siti Nuramira Abu Bakar, Daruliza Kernain, Razip Samian et al. "Relationship between the Structure and Electrical Conductivity of 12-Mer Single-Stranded Polyadenine Studied by Scanning Tunnelling Microscope." In Materials Science Forum, vol. 966, pp. 119-125. Trans Tech Publications Ltd (2019).
- Zaharim, Wan Nurfadhilah, Shukri Sulaiman, Saidah Sakinah Mohd Tajudin, Siti Nuramira Abu Bakar, Nur Eliana Ismail, Harison Rozak, and Isao Watanabe. "Basis Set Effects in Density Functional Theory Calculation of Muoniated Cytosine Nucleobase." In Key Engineering Materials, vol. 860, pp. 282-287. Trans Tech Publications Ltd (2020).

Keynote Speaker

- S. Sulaiman, Muon and Ageing. International Conference on Multidisciplinary Research (ICMR) 2016.
- I. Watanabe, Advanced Material Science Activities in Japan; International Conference on Magnetism and Its Application (ICMIA2019).
- I. Watanabe, Multi-Angle Approach to Magnetic Properties of Nano-State, 4th Padjadjaran International Physics Symposium (PIPS2019).

Invited talks

- S. Sulaiman, Understanding Electron Transport in DNA: μSR and First Principle Computational Investigations. URICAS Symposium 2017.
- S. Sulaiman Density Functional, Theory Study on Muonium Hyperfine Interaction in DNA Bases. RIKEN Symposium: International Workshop on Organic Molecular System 2018.
- I. Watanabe, What is the muon spin relaxation (□SR) and its applications for the solid state physics, 19th International Union of Material Research Societies International Conference in Asia 2018.
- I. Watanabe, How We can Approach to Magnetic Properties of Nano-State, The 1st International MIPAnet Conference on Science and Materials 2019.
- I. Watanabe, High Muon Sensitivity to Nano-Scale Magnetization, Invention and Innovation of New Concepts in the Field of Nano Science and Nanotechnology 2020.
- D.P. Sari and I. Watanabe, Volume Fraction Determination of Nanoscopic Partial Ordering by Muon, Invention and Innovation of New Concepts in the Field of Nano Science and Nanotechnology 2020.

Oral presentations

- DFT and μ SR Studies on Muon Sites in DNA. Postgraduate Colloquium 2017.
- Density Functional Theory Studies on Guanine and Cytosine. 7th ICMR Conference 2018.
- Observation of 12mer Single Strand DNA Oligomer by Using HRTEM. Postgraduate Colloquium 2018.
- DFT Studies on The Electronic Structures of 12mer Single Strand DNA Oligomers. URICAS Symposium 2019.
- The Study of Electrical Conductivity in 12-Mer Single-Stranded DNA by Muon- Spin Relaxation and Scanning Tunneling Microscopy. URICAS Symposium 2019.
- Observation and Simulation of 12mer Single Strand Guanine Oligomer. International Conference on Ageing 2019.
- First Principles Theory of Hyperfine Interactions in Guanine Nucleobase. 8th International Conference on Multidisciplinary Research 2018.
- An Application of μSR in Biology: The Electron Transfer in DNA. Material Research Meeting 2019.
- First Principles Theory of Hyperfine Interactions in Guanine Nucleobase. Material Research Meeting 2019.
- Anisotropy of Lower Critical Field in Organic Layered Superconductor, 4th Padjadjaran International Physics Symposium (PIPS2019).
- Poster presentations (including our related activities)
- Density Functional Theory Studies on Muon Sites in DNA. URICAS Symposium 2017.
- μSR Studies on Electron Dynamics in Guanine. URICAS Symposium 2017.
- Density Functional Theory Studies on Muon Sites in Deoxyguanylic acid and 9- Methylguanine. RIKEN Symposium: International Workshop on Organic Molecular System 2018.
- μSR Studies on Electron Dynamics in Guanine. RIKEN Symposium: International Workshop on Organic Molecular System 2018.
- DFT Studies on Muon Stopping Sites in 1-Methylthymine and Thymidine Monophosphate. RIKEN Symposium: International Workshop on Organic Molecular System.
- First Principle Study of Muonium Trapping in Deoxycytidine Monophosphate and 1-Methylcytosine. RIKEN Symposium: International Workshop on Organic Molecular System.
- μSR Study on Electron Dynamics in Single Strand Synthetic DNA. JPS Autumn Meeting 2017.
- μSR Studies on Electron Motion Along DNA Molecule. 2018 Autumn Meeting, The Physical Society of Japan.

- The Effects of Split Valence Basis Sets on Muon Hyperfine Interaction in Guanine Nucleobase and Nucleotides Structures. 4th ICFMS 2018 in conjunction with 2nd RIKEN Symposium: International Workshop on Organic Molecular System.
- Simulation and Observation of 12mer Single Strand Guanine Oligomer. URICAS Symposium 2019.
- The Study of Electrical Conductivity in 12-mer Single-Strand DNA by Scanning Tunneling Microscopy. URICAS Symposium 2019.
- The Study of Electrical conductivity in 12-Mer Single-Strand DNA by Muon Spectroscopy, Scanning Tunneling Microscopy and Density Functional Theory. International Conference on Ageing 2019.
- Basis Set Effects in Density Functional Theory Calculation of Muoniated Cytosine Nucleobase. 4th Padjadjaran International Physics Symposium 2019.
- Functional Effects in Density Functional Theory Calculation of Au13(SR)n nanocluster. 4th Padjadjaran International Physics Symposium 2019.
- The Effects of Split Valence Basis Sets on Muon Hyperfine Interaction in Guanine Nucleobase and Guanine Nucleotide Structures. Material Research Meeting 2019.
- Density Functional Theory Investigation of Muon Hyperfine Interactions in Au25SR18 Nanocluster. Material Research Meeting 2019.
- DFT and μSR Studies on YBa2Cu3O6 and La2CuO4. Material Research Meeting 2019.
- Functional Effect of Density Functional Theory Calculation of Au Nano Cluster, 4th Padjadjaran International Physics Symposium (PIPS2019).
- Spin Alignment Studies on the Muon Site Determinations, 4th Padjadjaran International Physics Symposium (PIPS2019).
- Inter-Grain Resistivity of High-TC Nano Particles Evaluated Four-Point Probe Method, 4th Padjadjaran International Physics Symposium (PIPS2019).
- Synthesis of Pyrocholore Polycrystal and Their Magnetic Properties Studied by
- SR, 4th Padjadjaran International Physics Symposium (PIPS2019)

mTOR Signalling

Team leaders

Dr Teh Aik Hong
Universiti Sains Malaysia
Centre for Chemical Biology

Dr Tamao Hisano
RIKEN
Center for Biosystems Dynamics Research

Team members

- Prof. Mohammed Razip Samian
- Dr Tengku Yasmin Putri; research officer
- Yeap Kean Heng; Master course student
- Syafiqah Diana; Master course student
- Melissa Lian Qianyue; Master course student

Scientific background

The mTOR signalling pathway, consisting of the two complexes mTORC1 and mTORC2, integrates diverse signals to regulate important cellular processes related to growth and ageing. The key component protein, mTOR, is a kinase, and its activity is downregulated when the regulatory protein DEPTOR binds to its FAT domain. Deregulation of this pathway is linked to cancer, diabetes and neurodegenerative diseases, while blocking mTOR's activity has been reported to extend lifespan in roundworm, fruit fly and mouse.

Recently, mTOR signalling has been reported to be stimulated by enzymatically degraded alginate, which has previously been shown to promote the growth of plant roots and clams. Alginate belongs to a group of polysaccharides containing negatively charged sugars, uronates, which are degraded into unsaturated oligouronates by their respective lyases. Unsaturated oligoalginates have been identified as the active compounds in promoting cellular growth. Pectate, another type of uronate, also exhibits bioactivity such as immunoregulatory, anti-inflammatory and antibacterial activities.

Project aim

We aim to study how DEPTOR binds to mTOR and inhibits its activity by solving the structure of the complex between DEDTOP and mTOR's FAT domain via X-ray crystallography. We also aim to investigate the bioactivity of unsaturated oligoalginates and oligopectates on model organisms and their mechanisms in stimulating mTOR signalling, as well as to characterise and determine the structures of pectate lyase and alginate lyase that produce the unsaturated oligouronates.

Executive summary of research results

Full-length DEPTOR and several truncated versions were constructed, purified, characterised and crystallised. DEPTOR was found to form a dimer, and crystallization screening has yielded several promising conditions which are being optimised at present. However, mTOR's FAT domain was insoluble;

neither truncations of this domain nor co-expression with DEPTOR improved its solubility. As the dimeric mTOR structure has been published, a model of the DEPTOR–mTOR is being constructed.

Unsaturated oligoalginates, prepared by alginate lyase, were observed to promote yeast growth and extended C. elegans lifespan. Interestingly, it also partially rescued the rough eye phenotype in a fruit fly model of Alzheimer's disease. A pectate lyase has been cloned, expressed and purified, and unsaturated oligopectates are being prepared for testing on the three organisms.

Short term outlook

We have performed an in-silico analysis on the interaction between mTOR and DEPTOR, and on the basis of DEPTOR characterisation modelled a complex in which DEPTOR's extended linker could bind to mTOR's kinase domain for successive phosphorylation.

Future direction of joint research

After characterising the bioactivity of unsaturated oligoalginates and oligopectates on the model organisms, we plan to further investigate how these unsaturated oligouronates affect mTOR signalling via transcriptomic and proteomic studies. We also plan to characterise enzymatically and structurally other types of uronate lyases to produce different oligouronates for their bioactivity comparison.

Student training and fostering of future academic leaders

- Syafiqah Diana binti Subandi, MSc candidate
- Melissa Qianyue Lian, MSc candidate
- Sim Pei Fang, MSc graduate
- Yeap Kean Heng, MSc graduate

Scientific results

Published and accepted manuscripts in refereed journals

- Insights into DEPTOR regulation from in silico analysis of DEPTOR complexes. Aik-Hong Teh, Kean-Heng Yeap, Tamao Hisano. 2020. Journal of Structural Biology.
- Structural basis for binding uronic acids by family 32 carbohydrate-binding modules. Aik-Hong Teh, Pei-Fang Sim, Tamao Hisano. 2020. Biochemical and Biophysical Research Communications.
- Enhancing yeast growth with carboxylates under multiple nutrient limitations. Yusof, Tengku Yasmin, Melissa Qianyue Lian, Eugene Boon Beng Ong, and Aik-Hong Teh. 2021. 3 Biotech.

Oral presentations

- 'Characterisation of mTOR signalling proteins and biological activity of alginate', URICAS Symposium 2019, USM, Malaysia.
- 'Structural studies of mTOR-DEPTOR complex of the ageing-regulating mTOR signalling pathway', RIKEN-USM Workshop for URICAS 2018, RIKEN, Japan.
- 'Structural studies of mTOR kinase domain and DEPTOR complex of the ageing-regulating mTOR signalling pathway', URICAS Symposium 2017, USM, Malaysia.

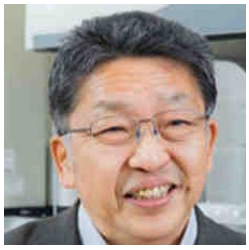
Poster presentations

- 'Characterisation and crystallisation of DEPTOR from the mTOR signalling pathway', International Conference on Ageing 2019: Ageing with Dignity, Penang, Malaysia.
- 'Characterisation of alginate lyase and biological activity of its products on model organisms', International Conference on Ageing 2019: Ageing with Dignity, Penang, Malaysia.

Ageing studies in yeast Saccharomyces cerevisiae

Team Leaders

Dr Eugene Ong
Universiti Sains Malaysia
Institute for Research in Molecular Medicine



Dr Nobumoto Watanabe
RIKEN
Centre for Sustainable Resource Science

Team members

- Dr Hiroyuki Osada, RIKEN
- Prof. Mohammed Razip Samian, USM
- Ong Tee Gee, MSc
- Mandy Kwong Mun Yee, MSc
- Lee Jee Whu, PhD, RIKEN IPA

Scientific background

Molecular senescence leads to impaired biochemical pathways that affect organismal ageing and lifespan in all organisms. In yeast, the chronological life span (CLS) is the measurement of the survival time of a population of non-dividing yeast cells during the stationary phase. Here, a CLS assay was used as an indicator of the maintenance of cell viability after it reaches the stationary phase, when the cells encounter nutrient starvation and halt reproduction (budding), to study senescence and cellular lifespan.

Project aim

This project aims to study the intracellular (proteins) and extracellular factors (natural compounds) that affect cellular lifespan using the yeast CLS assay. It is hypothesised that these factors can extend lifespan or delay ageing by modulating the molecular mechanisms of ageing-related pathways in yeast, thus will aid the further understanding of the ageing process.

Executive summary of research results

We have adapted a microplate-based method to perform yeast CLS assays to perform mass screening of age-related proteins and plant extracts (obtained from the USM-RIKEN Joint Laboratory for Bioprobe Discovery) to identify factors that may prolong the viability of yeast cells. From our protein screen, we were able to identify several age-related proteins and plant extracts that increased cell proliferation and are currently validating them further.

Short term outlook

Further characterisation of ageing-relatead proteins identified from the initial screen using site-directed mutagenesis and deletion strains to determine related pathways in yeast.

Future direction of joint research

In the future, small molecules from RIKEN's natural products library may be screened in the established yeast CLS and other assays. Dr Watanabe is also involved in Dr Eugene's other Fundamental Research Grant Scheme (FRGS) projects. An automated microplate reader is loaned to USM for carrying out yeast growth experiments and has contributed to data collection.

Student training and fostering of future academic leaders

- Lee Jee Whu, PhD
- Ong Tee Gee, MSc
- Mandy Kwong Mun Yee, MSc
- Ademola Adekoya (Attachment student from Prince of Songkla University, Thailand)

Scientific results

Published and accepted manuscripts in refereed journals

- Lee, J. W., Ong, T. G., Mohammed, R. S., Teh, A-H, Watanabe, N., Osada, H., & Ong, E. B. B. (2021). Screening of selected ageing-related proteins that extend chronological life span in yeast Saccharomyces cerevisiae. Scientific Reports, 11(24148).
- Kwong, M. M. Y., Lee, J. W., Mohammed, R. S., Habibah, A. W., Watanabe, N., Osada, H., & Ong, E. B. B. (2021). Identification of tropical plant extracts that extend yeast chronological life span. Cells, 10(10).
- Lee, J. W. & Ong, B. B. (2021). Genomic instability and cellular senescence: lessons from the budding yeast. Frontiers in Cell and Developmental Biology, 8.
- Kwong, M. Y., Lee, J. W., Mohammed, R. S., Watanabe, N., Osada, H., & Ong, B. B. (2019). Comparison of microplateand bottle-based methods to age yeast for chronological life span assays. Journal of Microbiological Methods, 167(105743).
- Adekoya, A.E., Chusri, S., Beng, E.O.B., Idowu, A.T. (2021). In vitro inhibitory potentials of Thai formulated polyherbal tea against oxidative stress promoters, Israel Journal of Plant Sciences, 162(26).
- Adekoya, A.E., Chusri, S., Boon Beng, E.O., Idown, A.T. (2021). Antioxidant Capacities of Traditionally Formulated Thai Herbal Decoction and Its Effect on Cell Growth Using Saccharomyces cerevisiae Model. Chiang Mai University Journal of Natural Sciences, 20(1).

Oral presentations

- 'Yeast as a model for ageing studies', URICAS Symposium 2017, USM, Malaysia.
- 'Development of CLS assay for screening of ageing-related proteins', RIKEN-USM Workshop for URICAS 2018, RIKEN, Japan.
- 'The humble yeast: An amazing model for drug discovery', 6th IPOPS, International Medical University, 2018
- 'Screening of ageing-related proteins', URICAS Symposium 2019, USM, Malaysia.
- 'Extending healthy lifespan: from yeast to humans', International Conference on Ageing 2019
- 'High throughput screening of plant extract on the chronological life span of Saccharomyces cerevisiae', International Conference on Ageing 2019
- 'Screening of Selected Ageing- Related Proteins that Extend Chronological Life Span in Yeast Saccharomyces cerevisiae', 4th International Conference on Molecular Biology & Biotechnology 2021

Poster presentations

- 'High-throughput Screen for Plant Extracts that Extend the Chronological Life Span of Ageing Yeast Saccharomyces cerevisiae', International Conference on Antioxidants and Degenerative Diseases (ICADD) 2018
- 'Development of a chronological life span assay for ageing studies in Saccharomyces cerevisiae', Ong TG, Samian MR, Watanabe N, Osada H, Ong EB, URICAS Symposium 2017

Transcriptome study of biofilm formation in Salmonella enteric subspecies enteric Serovar Typhi in the aged

Team leaders

Prof. Dr Phua Kia Kien
Universiti Sains Malaysia
Institute for Research in Molecular Medicine

Assoc. Prof. Dr Aziah Ismail
Universiti Sains Malaysia
Institute for Research in Molecular Medicine

Dr Todd Taylor
RIKEN
Center for Integrative Medical Sciences

Team members

- Jason Chin Khee Chian

Scientific background

Bacterial populations existing in symbiosis with our tissues play an important role in how metabolic processes interact to determine longevity. Asymmetries in cell growth and division occur in eukaryotes and prokaryotes alike. It has been shown that as a bacteria cell divides into two daughter cells, one daughter cell will inherit the old genetic material while the other receives the new genetic material. The study of bacterial aging is important, especially the fact that microbes' symbiotic relationship with the human body, where it have been proven that the age of the human gut microbiome affects nutrient absorbance and health of the human host. Not only that, the age of bacteria has been linked to its virulence and pathogenicity.

Project aim

Using next generation sequencing to study the transcriptome of bacteria as it ages will provide insights on how bacteria ages, and what the effect of aging does to the bacteria itself.

Executive summary of research results

Planktonic S. Typhi cells were cultured using standard nutrient broth whereas biofilm cells were cultured in a stressful environment using high shearing-force and bile to mimic the gallbladder. Sequencing libraries were prepared from S. Typhi planktonic cells and mature biofilm cells using the Illumina HiSeq 2500 platform, and the transcriptome data obtained were processed using Cufflinks bioinformatics suite of programmes to investigate differential gene expression between the two phenotypes. A total of 35 up-regulated and 29 down-regulated genes were identified. The identities of the differentially expressed genes were confirmed using NCBI BLAST and their functions were analyzed. The results showed that the genes associated with metabolic processes and biofilm regulations were down-regulated while those associated with the membrane matrix and antibiotic resistance were highly up-regulated.

Short term outlook

Research from this study had been published.

Student training and fostering of future academic leaders

One PhD student had graduated.

Scientific results

Published and accepted manuscripts in refereed journals

- Transcriptomic study of Salmonella enterica subspecies enterica serovar Typhi biofilm. Khee Chian Jason Chin, Todd Duane Taylor, Maxime Hebrard, Kogaan Anbalagan, Marjan Ganjali Dashti & Kia Kien Phua. 2017. BMC Genomics.

Oral presentations

- Optimization of Salmonella Typhi biofilm assay on polypropylene microtiter plates using response surface methodology, International congress of the Malaysian society for microbiology 2016
- Evaluation of Antifouling Activity of Polyhydroxyalkanoate and Sodium Alginate on Salmonella Typhi Biofilm Formation, International conference on beneficial microbes 2016
- A Study of Salmonella Pathogenicity Island (SPI)-Derived Non-Coding RNAs Regulation in S. Typhi Biofilm Formation, 15TH ASIAN CONFERENCE ON TRANSCRIPTION 2017 (ACT-XV 2017)
- A Study of Small Non-Coding RNAs of Salmonella enterica subspecies enterica serovar Typhi in Biofilm Development, 17th International Congress on Infectious Disease 2017
- Comparison Of Two Bioinformatic Methods For Transcriptomic Analysis Of Salmonella Typhi Biofilm Formation, URICAS Symposium 2017
- Transcriptome Study of Biofilm Formation in Salmonella enterica subspecies enterica serovar Typhi in Aging, URICAS Symposium 2018
- Whole-Genome SNP Genotyping and Survellance of the M DR Strain H58 from Salmonella Typhi Isolated from Kelantan, Malaysia from Year 2002 to 2012, URICAS Symposium 2019

Health Promotion Behaviour of Elderly

Team leader

Assoc. Prof. Dr Saidatulakmal Mohd
Universiti Sains Malaysia
School of Social Sciences

Team members

- Dr Abdul Rais Abdul Latiff, School of Social Sciences, USM

Scientific background

Health behavior is defined as behavior undertaken to promote or protect health (Brown and McCreedy 1986) and maintain health and quality of life (Simmons 1990). It is a behavior that is motivated by the desire for illness avoidance, early detection of illnesses, or maintains functioning within the constraints imposed by an illness, focusing on the positive potential for health (Pender, Murdaugh & Parsons 2002). Among the objectives of maintaining a positive health behavior are to promote independence, increase life expectancy and enhance quality of life (Resnick 2003) through modification of lifestyles. As commonly known changing lifestyles among elderly would decrease the prevalence of chronic disease among the aged, add years to their lives and diminish their demand for health services. In addition, health-promoting behaviors (HPB) is a key issue to prevent health declines and to promote physical functioning and quality of life of older people (Yeom 2013). The National Health and Morbidity Survey II (NHMSII 1996) indicated that the disease pattern among elderly had changed from diseases associated with ageing to disease associated with lifestyle i.e. hypertension, hypercholesterolemia, diabetes mellitus and adult asthma. Percentage of elderly total hospital admission has increased from 18.57% in 2005 to 20.37% in 2008 (Ministry of Health 2008) and it is expected that a majority of health care fund will go towards the elderly. Hence, one of the nation's biggest challenge in facing an aged society to how best to prevent and postpone diseases and disability and to maintain health, independence and mobility of the ageing population. In many developing countries, Malaysia included, little is known about current self-care practices, particularly among elderly (Irwan et al. 2016). Nevertheless, in general, elderly's negative perceptions or attitudes about ageing have been barriers to health- promoting behaviors (Palmore 2004). Elderly who had stronger negative perceptions regarding ageing were less likely to practice HPB.

Health-promoting lifestyles are series of behaviors, which guide an individual's family, community and society to improve peacefulness, happiness and realize health proficiency (Hua et al. 2015). HPBHPB follows the Health Promoting Lifestyle Profile II (HPLP II) developed by Walker and Hill (1996) includes items such as physical activities, health responsibility, interpersonal relations, self-actualization and stress management, measured on a Likert Scale ranging from 1 (never involved) to 4 (very much involved). The higher the total score, the healthier is the lifestyle.

Project aim

This project aims to achieve the following objectives:

- To determine degree of elderly's health promotion behaviors.
- To assess barriers to health-promoting behaviors.
- To empirically establish the relationship between elderly's health promotion behaviors and quality of life.
- To measure the factors that affect elderly's health promotion behaviors

Executive summary of research results

Health Promotion Behavior is defined as behavior undertaken to promote or protect health and maintain health and quality of life. It can be pointed to regular exercise, adequate sleep, avoiding alcohol and tobacco use, proper nutrition, avoidance of obesity, age-appropriate vaccinations, medical care, and avoidance of stresses.

The data on Health Promotion Behaviors show that:

- 14.4 percent of Malaysian elderly involve in smoking habit
- 52.7 percent of them involve in physical activity
- 6.5 percent of them are taking adequate fruits and vegetables.
- Common diseases found in Malaysian elderly are:
    - Depression (23%)
    - Hypertension (69%)
    - Hypercholesterolemia (65%)
    - Diabetes (5.7%).

Significant variables influencing health promotion behavior are gender, location, education and income. Female elderly with high education and income living in urban involve more in health promotion behavior than the other groups. There is no significant relationship between Health promotion behavior and quality of life for data in both 2011 and 2015.

Short term outlook

- Saidatulakmal Mohd, Norhafiza Mohd Sharif & Abdelhak Senadjki. Forthcoming. Health Promotion Behaviors and Quality of Life: A Cross Sectional Survey, Jurnal Ekonomi Malaysia
- Saidatulakmal Mohd, Norhafiza Mohd Sharif & Abdelhak Senadjki. Forthcoming. Health Promotion Behaviors among Elderly: A Case Study in Georgetown, Penang. Jurnal Ekonomi Malaysia

Future direction of joint research

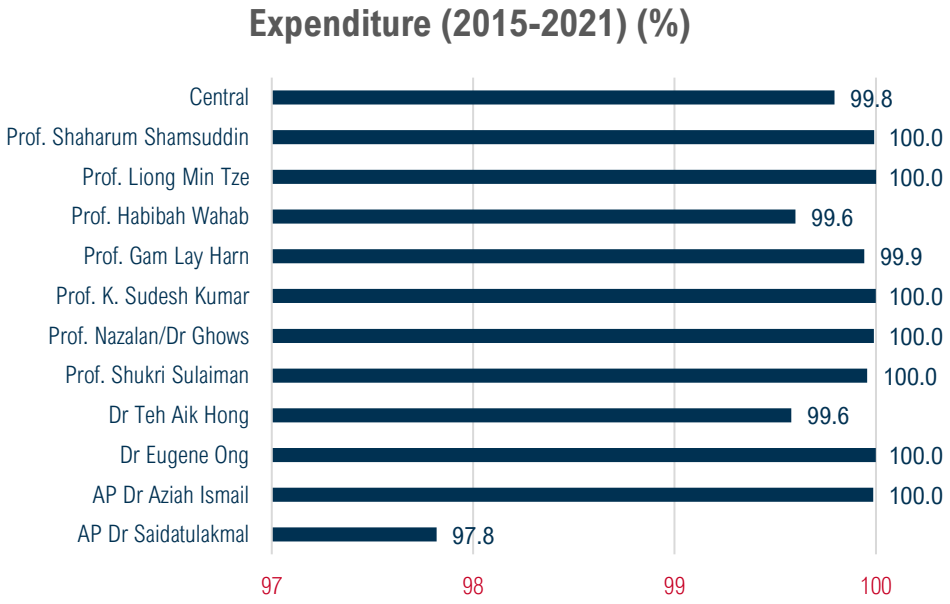
- To further analyzed survey data of 622 elderly in George Town, Melaka and Perak to empirically assess elderly's health promotion behaviour.
- Scientific results
- Psychological Wellbeing, Health and Ageing - Elder Abuse and Neglect. Saidatulakmal Mohd, Rose Jacob. 2017. Journal of Aging and Neuropsycology.
- Active Ageing In Malaysia: Case Study In Georgetown. Saidatulakmal Mohd, Norhafiza Md Sharif. 2020. Conference: 8th International Conference on Multidisciplinary Research 2019.
- Ethnic Variability of Health-Promoting Behaviours of Older Adults in Malaysia. Mohd, Saidatulakmal, Abdul Rais Abdul Latiff, Radieah Mohd Noor, and Sharifah Nurlaili Farhana Syed Azhar. 2022. Journal of Population Ageing, 1-21.
- Mohd. S., Senadjki, A. & Abdul Latiff, A.R.. 2022. Poverty and Elderly's Health. In. R. Baikady, J. Gal, S. M. Sajid, V. Nadesan & G. Jianguo (Eds.), The Routledge Handbook of poverty in the Global South. Routledge.

Oral presentations

- 'Elder Abuse and Neglect in the Family – Voices of the Abused', 2nd USM International Conference on Social Sciences (ICOSS). 23-25 Aug 2017, The Gurney Hotel & Residences, Penang, Malaysia
- 'Psychological well-being, health and ageing – Elder abuse and neglect, a silent cry', 19th International Conference on Mental Health, 21-22 May 2017, Berlin Germany
- 'Health Promotion Behaviors and Quality of Life of Elderly – A Cross Sectional Survey, Findings', RIKEN-USM Workshop for URICAS, 1 – 2 February 2018, Wako, Japan.
- 'Spirituality, Stress Management and Self-Efficacy among Elderly with Hypertension – Case Study of Elderly in Penang, Perak and Melaka', USM- RIKEN Symposium, 6 March 2019 USM

2.3 Budget and Expenditure

URICAS was provided a budget of RM 5,000,000.00 for the entire duration of the project 2015-2021. RM 2,500,000.00 was allocated for the research budget of the joint projects. The RM 2,500,000.00 central operating budget was used to support the wages of postdoctoral fellows, graduate student assistants, research officers, research assistants; and to conduct and organise all joint meetings, community activities, training workshops and engagement. The total expenditure was RM 4,991,363 (99.83%).



3.0 Overall Milestone Achievements

3.1 Overall Research Outputs

All URICAS's teams made remarkable contributions in publications. A total of 76 papers (Figure 6, Table 3) were published with 71 papers in SCOPUS indexed journals, 56 papers in The Institute for Scientific Information - Web of Science (ISI/WOS) indexed journals and 5 more in other journals. Throughout the 5-year period, URICAS produced one paper in 2015, three papers in 2017, four more in 2018, 21 papers in 2019, 24 papers in 2020 and 23 papers were published in 2021. Regarding the Journal Citation Ranking and Quartile Scores, URICAS has 18 papers in Quartile 1 (Q1), 28 papers in Quartile 2 (Q2), nine papers in Quartile 3 (Q3), six in Quartile 4 (Q4) and 15 more in other citation rankings.

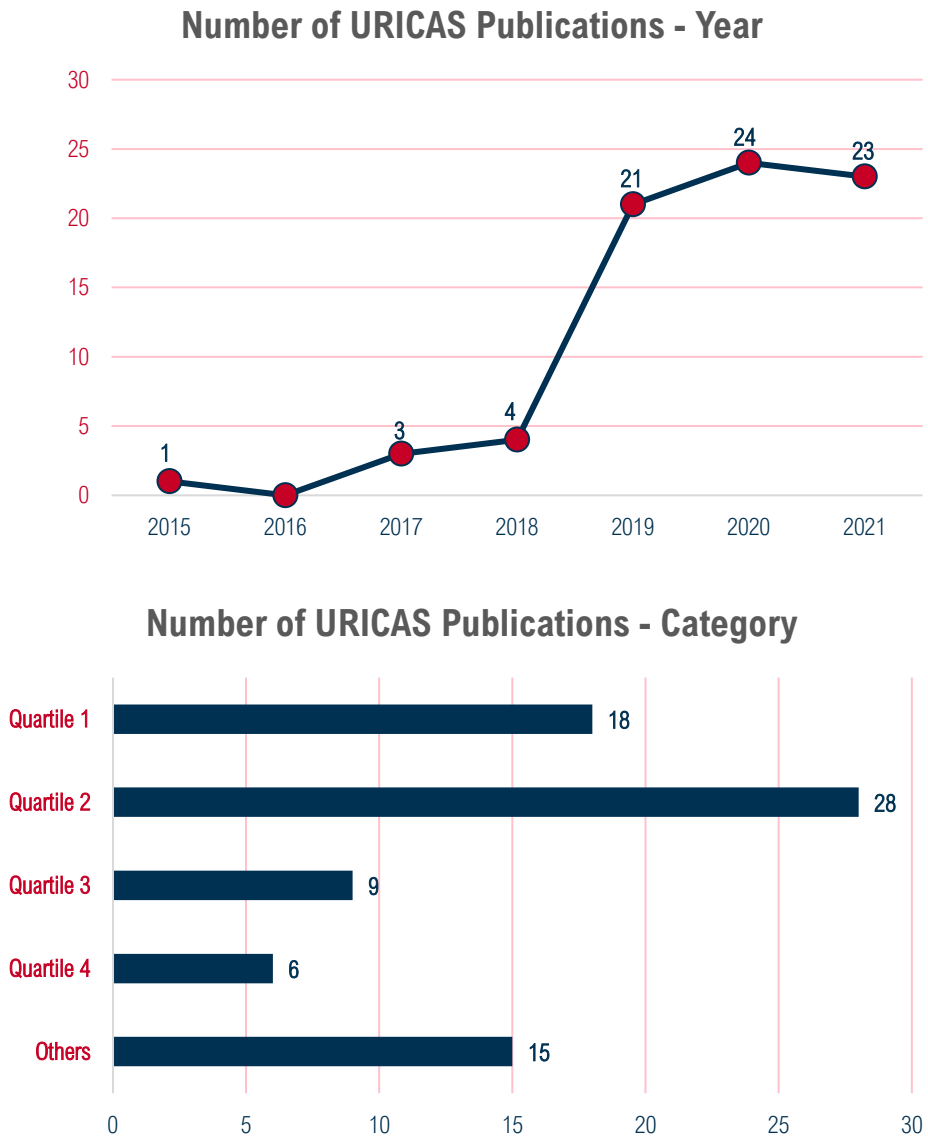


Figure 6: Papers published by URICAS teams.

Table 3: List of published papers from URICAS (2015-2021).

	List of Authors	Publication Title	Journal
1.	Nurul Fatihah Mohamad Nasir; Azalina Zainuddin; Shaharum Shamsuddin	Emerging Roles of Sirtuin 6 in Alzheimer's Disease	Journal Of Molecular Neuroscience
2.	Nor Shaheera Mohamad Kamal, Sabreena Safuan, Shaharum Shamsuddin, Parisa Foroozandeh	Aging of the cells: Insight into cellular senescence and detection Methods	European Journal Of Cell Biology
3.	Siti Asmaa Mat Jusoh, Parisa Foroozandeh, Lee Yan Fen, Mardani Abdul Halim, Manoj Kumar Laskmanan and Shaharum Shamsuddin	COVID-19 Mini-Review: D614G Mutation as an Independent Risk-Factor to the Expression of ACE2 and DPP4 Associated Increased Severity in COVID-19	Sains Malaysiana
4.	Lakshmanan, M., Foong, C.P., Abe, H. Sudesh, K.	Biosynthesis and characterization of co and ter-polyesters of polyhydroxyalkanoates containing high monomeric fractions of 4-hydroxybutyrate and 5-hydroxyvalerate via a novel PHA synthase	Polymer Degradation And Stability
5.	Idris Zainab-L, Sudesh, K.	High cell density culture of Cupriavidus necator H16 and improved biological recovery of polyhydroxyalkanoates using mealworms	Journal Of Biotechnology
6.	Shaik Ling Ang, Bakiah Shaharuddin, Jo-Ann Chuah, Kumar Sudesh	Electrospun poly(3-hydroxybutyrate-co-3-hydroxyhexanoate)/silk fibroin film is a promising scaffold for bone tissue engineering	International Journal Of Biological Macromolecules
7.	Noor-Afiqah Ahmad Zain, Lee-Mei Ng, Choon Pin Foong, Yen Teng Tai, Jayaram Nanthini, Kumar Sudesh	Complete Genome Sequence of a Novel Polyhydroxyalkanoate (PHA) Producer, *Jeongeupia* sp. USM3 (JCM 19920) and Characterization of Its PHA Synthases	Current Microbiology
8.	Shaik Ling Ang, Ramamoorthi Sivashankari, Bakiah Shaharuddin, Jo-Ann Chuah, Takeharu Tsuge, Hideki Abe, Kumar Sudesh	Potential Applications of Polyhydroxyalkanoates as a Biomaterial for the Aging Population	Polymer Degradation And Stability
9.	Yan-Fen Lee, Nanthini Sridewi, Surash Ramanathan and Kumar Sudesh	The influence of electrospinning parameters and drug loading on polyhydroxyalkanoate (PHA) nanofibers for drug delivery	International Journal Of Biotechnology
10.	Choon Pin Foong, Manoj Lakshmanan, Hideki Abe, Todd D. Taylor, Swee Yeok Foong & Kumar Sudesh	A novel and wide substrate specific polyhydroxyalkanoate (PHA) synthase from unculturable bacteria found in mangrove soil	Journal Of Polymer Research

11.	Pulingam, Thiruchelvi, Thaigarajan Parumasivam, Amirah Mohd Gazzali, Azlinah Mohd Sulaiman, Jiun Yee Chee, Manoj Lakshmanan, Chai Fung Chin, and Kumar Sudesh	Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome	European Journal Of Pharmaceutical Sciences
12.	Demirdöğen, Ruken Esra, Fatih Mehmet Emen, Kasim Ocakoglu, Paramasivam Murugan, Kumar Sudesh, and Göktürk Avşar	Green Nanotechnology for Synthesis and characterization of poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) nanoparticles for sustained bortezomib release using supercritical CO2 assisted particle formation combined with electrodeposition	International Journal Of Biological Macromolecules
13.	Florence Tan Hui Ping, Ghows Azzam	*Drosophila melanogaster* - Deciphering Alzheimer's disease	Malaysian Journal Of Medical Sciences
14.	Azali Azlan, Mardani Abdul Halim, Ghows Azzam	Genome-wide identification and characterization of long intergenic noncoding RNAs in the regenerative flatworm *Macrostomum lignano*	Genomics
15.	Guoxia LIU, Florence Hui-Ping TAN, Sie-Yik Amy LAU, Mohamad Hafis JAAFAR, Fiona Yi-Li CHUNG, Ghows AZZAM, Min-Tze LIONG, Yin LI	Lactic acid bacteria feeding reversed the malformed eye structures and ameliorated gut microbiota profiles of *Drosophila melanogaster* Alzheimer's Disease model	Journal Of Applied Microbiology
16.	Mardani Abdul Halim, Florence Hui Ping Tan, Azali Azlan, Ian Ilham Rasyid, Nurlina Rosli, Shaharum Shamsuddin, Ghows Azzam	Ageing, Drosophila melanogaster and Epigenetics	Malaysian Journal Of Medical Sciences
17.	Yuen Chee Wah, Mardani Abdul Halim, Nazalan Najimudin, Ghows Azzam	Effects of Salvianolic Acid A On Β-Amyloid Mediated Toxicity In *Caenorhabditis Elegans* Model Of Alzheimer's Disease	Journal Of Biomedical And Clinical Sciences
18.	Chee Wah Yuen, Vikneswaran Murugaiyah, Nazalan Najimudin, GhowsAzzam	Danshen (*Salvia miltiorrhiza*) water extract shows potential neuroprotective effects in Caenorhabditis elegans	Journal Of Ethnopharmacology
19.	Tan, F.H.P., Hadri, N.A.B., Najimudin, N., Watanabe, N. and Azzam, G.	Ethyl caffeate ameliorated amyloid-beta42 protein-associated toxicity in PC12 cells and Drosophila melanogaster	Geriatrics & Gerontology International
20.	Tan, F.H.P., Ting, A.C.J., Leow, B.G., Najimudin, N., Watanabe, N. and Azzam, G.	Alleviatory effects of Danshen, Salvianolic acid A and Salvianolic acid B on PC12 neuronal cells and Drosophila melanogaster model of Alzheimer's disease	Journal Of Ethnopharmacology
21.	Lye HS, Kato T, Low WY, Taylor TD, Prakash T, Lew LC, Ohno H, Liong MT	*Lactobacillus fermentum* FTDC 8312 combats hypercholesterolemia via alteration of gut microbiota	Journal Of Biotechnology

22.	Lee-Ching Lew, Sy-Bing Choi, Boon-Yin Khoo, Sasidharan Sreenivasan, Kee-Leong Ong, and Min-Tze Liong	*Lactobacillus plantarum* DR7 Reduces Cholesterol via Phosphorylation of AMPK That Down-regulated the mRNA Expression of HMG-CoA Reductase	Korean Journal For Food Science Of Animal Resources
23.	Ong JS, Taylor TD, Wong CB, Khoo BY, Sasidharan , Choi SB, Ohno H, Liong MT	Extracellular transglycosylase and glyceraldehyde-3-phosphate dehydrogenase attributed to the anti-staphylococcal activity of *Lactobacillus plantarum* USM8613	Journal Of Biotechnology
24.	Ong JS, Taylor TD,Yong CC, Khoo BY, Sasidharan , Choi SB, Ohno H, Liong MT	*Lactobacillus plantarum* USM8613 Aids in Wound Healing and Suppresses Staphylococcus aureus Infection at Wound Sites	Probiotics And Antimicrobial Proteins
25.	Lew LC, Hor YY, Jaafar MH, Lau ASY, Khoo BY, Sasidharan S, Choi SB, Ong KL, Kato T, Nakanishi Y, Ohno H, Liong MT	Effects of Potential Probiotic Strains on the Fecal Microbiota and Metabolites of D-Galactose-Induced Aging Rats Fed with High-Fat Diet	Probiotics And Antimicrobial Proteins
26.	Lew LC, Hor YY, Jaafar MH, Lau ASY, Ong JS, Chuah LC, Yap KP,Ghows A, Azali A, Liong MT	*Lactobacilli* modulated AMPK activity and prevented telomere shortening in ageing rats	Beneficial Microbes
27.	Hor YY, Lew LC, Jaafar MH, Lau ASY,Ong JS, Kato T, Nakanishi Y, Ghows A, Azali A, Ohno H, Liong MT	*Lactobacillus* sp. improved microbiota and metabolite profiles of aging rats	Pharmacological Research
28.	Hor YY, Ooi CH, Khoo BY, Choi SY, Seeni A, Shaharum S, Oon CE, Ong KL, Jeong WS, Liong MT	*Lactobacillus* Strains Alleviated Aging Symptoms and Aging-Induced Metabolic Disorders in Aged Rats	Journal Of Medicinal Food
29.	Tan F.H.P., Liu G., Lau S.-Y.A., Jaafar M.H., Park Y.-H., Azzam G., Li Y., Liong M.-T. 2020.	*Lactobacillus* probiotics improved the gut microbiota profile of a *Drosophila melanogaster* Alzheimer's disease model and alleviated neurodegeneration in the eye.	Beneficial Microbes
30.	Ahmad Imran Zaydi , Lee-Ching Lew , Yan-Yan Hor , Mohamad Hafis Jaafar , Li-Oon Chuah , Kien-Pong Yap, Azali Azlan, Ghows Azzam, Min-Tze Liong.	*Lactobacillus plantarum* DR7 improved brain health in aging rats via the serotonin, inflammatory and apoptosis pathways	Beneficial Microbes
31.	Lee-Ching Lew, Yan-Yan Hor , Mohamad-Hafis Jaafar , Amy-Sie-Yik Lau, Boon-Kiat Lee , Li-Oon Chuah , Kien-Pong Yap , Azali Azlan , Ghows Azzam, Sy-Bing Choi, Min-Tze Liong.	*Lactobacillus* Strains Alleviated Hyperlipidemia and Liver Steatosis in Aging Rats Via Activation of AMPK.	International Journal Of Molecular Sciences
32.	Y.-Y. Hor C.-H. Ooi L.-C. Lew M.H. Jaafar A.S.-Y. Lau B.-K. Lee A. Azlan S.-B. Choi G. Azzam M.-T. Liong	The molecular mechanisms of probiotic strains in improving ageing bone and muscle of d-galactose-induced ageing rats	Journal Of Applied Microbiology

33.	Ho Yueng Hsing, Selestin A/P Rathnasamy, Habibah A Wahab	Docking-based virtual screening in search of natural PTP1B inhibitors in treating Type-2 diabetes mellitus and obesity	Biomedical Research And Therapy
34.	Kesevan Rajah Kumaranb, Mohamad Anuar Ahada, Mira Syahfriena Amir Rawab, Habibah Wahabb, Zurina Hassan	Potential Malaysian medicinal plants for the treatment of Alzheimer's disease	Australian Herbal Insight
35.	Maywan Hariono, Rina F. Nuwarda, Muhammad Yusuf, Rollando Rollando, Riris I. Jenie, Belal Al-Najjar, Jeffry Julianus, Kevin C. Putra, Ervan S. Nugroho, Yohanes K. Wisnumurti, Sangga P. Dewa, Benedictus W. Jati, Reynaldo Tiara, Ratna D. Ramadani, Lailatul Qodria, and Habibah A. Wahab	Arylamide as Potential Selective Inhibitor for Matrix Metalloproteinase 9 (MMP9): Design, Synthesis, Biological Evaluation, and Molecular Modeling	Journal Of Chemical Information And Modeling
36.	Florentinus D O Riswanto, Mira S A Rawa, Vikneswaran Murugaiyah, Nurul H Salin, Enade P Istyastono, Maywan Hariono, Habibah A Wahab	Anti-Cholinesterase Activity of Chalcone Derivatives: Synthesis, In vitro Assay and Molecular Docking Study	Medicinal Chemistry
37.	Mira Syahfriena, Zurina Hassan, Vikneswaran Murugaiyah, Toshihiko Nogawa	Anti-cholinesterase potential of diverse botanical families from Malaysia: Evaluation of crude extracts and fractions from liquid-liquid extraction and acid-base fractionation	Journal Of Ethnopharmacology
38.	Nurul Amira Nurul Azman, Maram B. Alhawarri, Mira Syahfriena Amir Rawa, Roza Dianita, Amirah Mohd Gazzali, Toshihiko Nogawa and Habibah A. Wahab	Potential Anti-Acetylcholinesterase Activity of *Cassia timorensis* DC	Molecules
39.	Maywan Hariono, Rollando Rollando, Jasson Karamoy,Pandu Hariyono, M. Atmono, Maria Djohan, Wiwy Wiwy, Rina Nuwarda, Christopher Kurniawan, Nurul Salin andHabibah Wahab	Bioguided Fractionation of Local Plants against Matrix Metalloproteinase9 and Its Cytotoxicity against Breast Cancer Cell Models: *In Silico* and *In Vitro* Study	Molecules
40.	Ninie Nadia Zulkipli, Rahimah Zakaria, Idris Long, Siti Fadilah Abdullah, Erma Fatiha Muhammad, Habibah A. Wahab, and Teguh Haryo Sasongko	In Silico Analyses and Cytotoxicity Study of Asiaticoside and Asiatic Acid from Malaysian Plant as Potential mTOR Inhibitors	Molecules

41.	Mohamad Anuar Ahad, Kesevan Rajah Kumaran, Tiang Ning, Nur Izzati Mansor, Mohamad Azmeer Effendy, Thenmoly Damodaran, Kamilla Lingam, Habibah Abdul Wahab, Norshariza Nordin, Ping Liao, Christian P Müller, Zurina Hassan	Insights into the neuropathology of cerebral ischemia and its mechanisms	Reviews In Neurosciences
42.	Nurul Hanim Salin ,Rahmah Noordin ,Belal O. Al-Najjar,Ezatul Ezleen Kamarulzaman,Muhammad Hafiznur Yunus,Izzati Zahidah Abdul Karim,Nurul Nadieya Mohd Nasim,Iffah Izzati Zakaria, Habibah A. Wahab	Identification of potential dual -targets anti- toxoplasma gondii compounds through structure-based virtual screening and in-vitro studies	Plos One
43.	Mira Syahfriena Amir Rawa, Toshihiko Nogawa Akiko Okano, Yushi Futamura, Takemichi Nakamura, Habibah A Wahab, Hiroyuki Osada	A new peptaibol, RK-026A, from the soil fungus *Trichoderma* sp. RK10-F026 by culture condition-dependent screening	Bioscience, Biotechnology, And Biochemistry
44.	Alhawarri, Maram B., Roza Dianita, Khairul Niza Abd Razak, Suriani Mohamad, Toshihiko Nogawa, and Habibah A. Wahab	Antioxidant, Anti-Inflammatory, and Inhibition of Acetylcholinesterase Potentials of Cassia timoriensis DC. Flowers	Molecules
45.	Fatiha Muhammad, Erma, Ashutosh Kumar, Habibah A. Wahab, and Kam YJ Zhang	Identification of 1, 2, 4-Triazolylthioethanone Scaffold for the Design of New Acetylcholinesterase Inhibitors	Molecular Informatics
46.	Kumaran, Kesevan Rajah, Habibah Abdul Wahab, and Zurina Hassan	In vitro anti-cholinesterase activity and in vivo screening of Coccoloba uvifera, Mimusops elengi and Syzygium aqueum extracts on learning and memory function of chronic cerebral hypoperfusion rat	Neuroscience Research Notes
47.	Rawa, Mira Syahfriena Amir, Toshihiko Nogawa, Akiko Okano, Yushi Futamura, Habibah A. Wahab, and Hiroyuki Osada	Zealpeptaibolin, an 11-mer cytotoxic peptaibol group with 3 Aib-Pro motifs isolated from Trichoderma sp. RK10-F026	The Journal Of Antibiotics
48.	Amir Rawa, Mira Syahfriena, Nurul Amira Nurul Azman, Suriani Mohamad, Toshihiko Nogawa, and Habibah A. Wahab	In Vitro and In Silico Anti-Acetylcholinesterase Activity from Macaranga tanarius and Syzygium jambos	Molecules
49.	Han Li, Badrul Hisham Yahaya, Wai Hoe Ng, Narazah Mohd Yusoff and Juntang Lin	Conditioned Medium of Human Menstrual Blood-Derived Endometrial Stem Cells Protects Against MPP+-Induced Neurotoxicity In Vitro	Frontiers In Molecular Neuroscience

50.	Noridzzaida Ridzuan, Norashikin Zakaria, Darius Widera, Jonathan Sheard, Mitsuru Morimoto, Hirofumi Kiyokawa, Seoparjoo Azmel Mohd Isa, Gurjeet Kaur Chatar Singh, Kong-Yong Then, Ghee-Chien Ooi, Badrul Hisham Yahaya	Human Umbilical Cord Mesenchymal Stem Cell Derived Extracellular Vesicles Ameliorate Airway Inflammation in a Rat Model of chronic obstructive pulmonary disease (COPD)	Stem Cell Research And Therapy
51.	Jie Lian, Juntang Lin, Norashikin Zakaria, Badrul Hisham Yahaya	Acute Lung Injury: Disease Modelling and the Therapeutic Potential of Stem Cells	Advances In Experimental Medicine And Biology
52.	Nazilah Abdul Satar, Mohd Nazri Ismail and Badrul Hisham Yahaya	Synergistic Roles of Curcumin in Sensitising the Cisplatin Effect on a Cancer Stem Cell-Like Population Derived from Non-Small Cell Lung Cancer Cell Lines	Molecules
53.	Aik-Hong Teh, Kean-Heng Yeap, Tamao Hisano	Insights into DEPTOR regulation from in silico analysis of DEPTOR complexes	Journal Of Structural Biology
54.	Aik-Hong Teh, Pei-Fang Sim, Tamao Hisano	Structural basis for binding uronic acids by family 32 carbohydrate-binding modules	Biochemical And Biophysical Research Communications
55.	Yusof, Tengku Yasmin, Melissa Qianyue Lian, Eugene Boon Beng Ong, and Aik-Hong Teh	Enhancing yeast growth with carboxylates under multiple nutrient limitations	3 Biotech
56.	Ying-Hui Teh, Xuan-Yi Sim, Yan-Fen Lee, Waqas Ahmad, Vikneswaran Murugaiyah, Baharudin Ibrahim, Mohd Nazri Ismail, Peter Greimel, Lay-Harn Gam	Urinary protein profile changes in diabetic rats and pre-diabetic rats fed with high-fat diets	Biomedical Research And Therapy
57.	Yan-Fen Lee, Xuan-Yi Sim, Ying-Hui Teh, Mohd Nazri Ismail, Peter Greimel, Vikneswaran Murugaiyah, Baharudin Ibrahim, Lay-Harn Gam	The effects of high-fat diet and metformin on urinary metabolites in diabetes and prediabetes rat models	Biotechnology And Applied Biochemistry
58.	Ying-Hui Teh, Xuan-Yi Sim, Yan-Fen Lee, Waqas Ahmad, Vikneswaran Murugaiyah, Baharudin Ibrahim, Mohd Nazri Ismail, Peter Greimel, Lay-Harn Gam	Potential Urinary disease Marker for Diabetes	Biomedical Journal Of Scientific And Technical Research

59.	Xuan-Yi Sim, Waqas Ahmad, Yan-Fen Lee, Ying-Hui Teh, Vikneswaran Murugaiyah, Baharudin Ibrahim, Peter Greimel, Lay-Harn Gam	Weight Gain and Adipose Tissue Accumulation in Diabetic and Prediabetic Rats Fed with Palm Olein enriched High Fat Diet	Journal Of Biochemistry, Microbiology And Biotechnology
60.	Sim Xuan-Yi, Baharudin Ibrahim, and Lay-Harn Gam	Urinary metabolites of type 2 diabetes rats fed with palm oil-enriched high fat diet	Heliyon
61.	Lee Yan Fen, Gam Lay Harn, Sim Xuan Yi, Mohd Nazri Bin Ismail	Overexpression of Hsc 70 and pyruvate dehydrogenase in the brain tissue at the early stage of high fat diet consumption	HAYATI Journal Of Biosciences
62.	Khee Chian Jason Chin, Todd Duane Taylor, Maxime Hebrard, Kogaan Anbalagan, Marjan Ganjali Dashti & Kia Kien Phua	Transcriptomic study of Salmonella enterica subspecies enterica serovar Typhi biofilm	BMC Genomics
63.	Mandy Mun Yee Kwong, Jee Whu Lee, Mohammed Razip Samian, Nobumoto Watanabe, Hiroyuki Osada, Eugene Boon Beng Ong	Comparison of microplate- and bottle-based methods to age yeast for chronological life span assays	Journal Of Microbiological Methods
64.	Lee, Jee Whu, Tee Gee Ong, Mohammed Razip Samian, Aik-Hong Teh, Nobumoto Watanabe, Hiroyuki Osada, and Eugene Boon Beng Ong	Screening of selected ageing-related proteins that extend chronological life span in yeast *Saccharomyces cerevisiae*	Scientific Reports
65.	Kwong, Mandy Mun Yee, Jee Whu Lee, Mohammed Razip Samian, Habibah A Wahab, Nobumoto Watanabe, and Eugene Boon Beng Ong	Identification of tropical plant extracts that extend yeast chronological life span	Cells
66.	Lee, Jee Whu, and Eugene Boon Beng Ong	Genomic instability and cellular senescence: lessons from the budding yeast	Frontiers In Cell and Developmental Biology
67.	Harison Rozak, Wan Nurfadhilah Zaharim, Issei Miyazaki, Nur Eliana Ismail, Siti Nuramira Abu Bakar, Daruliza Kernain, Razip Samian, Koichi Ichimura, Mohamed Ismail, Mohamed-Ibrahim, ,Shukri Sulaiman, and Isao Watanabe	Relationship Between the Structure and Electrical Conductivity of 12-Mer Single-Stranded Polyadenine Studied by Scanning Tunnelling Microscope	Materials Science Forum

68.	Wan Nurfadhilah Zaharim, Shukri Sulaiman, Siti Nuramira Abu Bakar, Nur Eliana Ismail, Harison Rozak, Isao Watanabe	The Effects of Split Valence Basis Sets on Muon Hyperfine Interaction in Guanine Nucleobase and Nucleotide Structures	Materials Science Forum
69.	Muhammad Redo Ramadhan, Irwan Ramli, Muhammad Darwis Umar, Suci Winarsih, Dita Puspita Sari, Azwar Manaf, Budhy Kurniawan, Mohamed Ismail Mohamed-Ibrahim, Shukri Sulaiman, Isao Watanabe	Effects of the Supercell's Size on Muon Positions Calculations of La2CuO4	Materials Science Forum
70.	Irwan Ramli, Saidah Sakinah Mohd Tajudin, Muhammad Redo Ramadhan, Dita Puspita Sari, Shukri Sulaiman, Mohamed Ismail Mohamed-Ibrahim, Budi Kurniawan, Isao Watanabe	Magnetic Properties of YBa2Cu3O6 Studied by Density Functional Theory Calculation	Materials Science Forum
71.	Muhammad Redo Ramadhan, Irwan Ramli, Dita Puspita Sari, Budhy Kurniawan, Azwar Manaf, Mohamed Ismail Mohamed-Ibrahim, Shukri Sulaiman, Isao Watanabe	Spin Alignment Studies on the Muon-Site Determination in La2CuO4	Key Engineering Materials
72.	Julia Angel, Retno Asih, Hironori Nomura, Tomoya Taniguchi, Kazuyuki Matsuhira, Muhammad Redo Ramadhan, Irwan Ramli, Makoto Wakeshima, Yukio Hinatsu, Mohamed Ismail Mohamed-Ibrahim8, Shukri Sulaiman, Isao Watanabe	Magnetic Properties of Hole-Doped Pyrochlore Iridate (Y1-x-yCuxCay)2Ir2O7	Materials Science Forum
73.	Wan Nurfadhilah Zaharim, Shukri Sulaiman, Saidah Sakinah Mohd Tajudin, Siti Nuramira Abu Bakar, Nur Eliana Ismail, Harison Rozak, Isao Watanabe	Basis Set Effects in Density Functional Theory Calculation of Muoniated Cytosine Nucleobase	Key Engineering Materials
74.	Zaharim, Wan Nurfadhilah, Harison Rozak, Shukri Sulaiman, Siti Nur Afifi Ahmad, Dang Fatihah Hasan Baseri, Saidah Sakinah Mohd-Tajudin, Ang Lee Sin, and Isao Watanabe	Density Functional Theory Investigation of Hyperfine Interaction in DNA Nucleobase and Nucleotide Muoniated Radicals	Journal Of The Physical Society Of Japan
75.	Zaharim, Wan N., Siti NA Ahmad, Shukri Sulaiman, Harison Rozak, Dang F. Hasan Baseri, Nur A. Mohamad Rosli, Saidah S. Mohd-Tajudin, Lee S. Ang, and Isao Watanabe	Density Functional Theory Study of 12mer Single-Strand Guanine Oligomer and Associated Muon Hyperfine Interaction	ACS Omega
76.	Mohd, Saidatulakmal, Abdul Rais Abdul Latiff, Radieah Mohd Noor, and Sharifah Nurlaili Farhana Syed Azhar	Ethnic Variability of Health-Promoting Behaviours of Older Adults in Malaysia	Journal Of Population Ageing

3.2 External Grants

In addition to publishing papers, URICAS teams have successfully secured grants from external sources throughout the 5 years (Table 4). The types of research grants include Trans Disciplinary Research Grant Scheme (TRGS), Prototype Research Grant Scheme (PRGS), Fundamental Research Grant Scheme (FRGS), as well as grants from external agencies. The total funding received by URICAS teams is estimated to be **RM 2,317,767.00**.

Table 4: List of external grants secured by URICAS members.

Project leader	Project title	Type of grant	Funding agency	Starting year	Tenure (years)	Total funding
Shaharum Shamsuddin	Deciphering the role of long non-coding RNA (lncRNA) and transcriptome wide mapping of RNA m6A methylation in ageing *Drosophila melanogaster*	FRGS	Kementerian Pendidikan Malaysia	2019	2	165,700.00
Shaharum Shamsuddin	Elucidating the effects of *Clinacanthus nutans lindau* extract in delaying or slowing down ovarian aging through antioxidant property	External Agency	Malaysia Toray Science Foundation (MTSF)	2020	2	20,000.00
Shaharum Shasuddin	Explicating of Novel Pathwaysof THICAPA and POET in Different Genetic Backgrounds of Alzheimer's Disease Human Cell Lines	TRGS	Kementerian Pengajian Tinggi	2020	3	363,600.00
Shaharum Shamsuddin	Development of Nucleic Acid Lateral Flow Assay for Influenza A and Covid-19: A New Rapid & Sensitive Test for Poultry Industry in Malaysia	PRGS	Kementerian Pengajian Tinggi	2020	2	283,301.00
Shukri Sulaiman	Effect of Methylation on Electron Transport in Double Strand DNA	External Agency	Newton Fund & MYPAIR	2020	2	358,416.00
Ghows Azzam	Deciphering the mechanism of CTP synthase-induced tumour growth in Drosophila melanogaster	FRGS	Kementerian Pendidikan Malaysia	2019	3	247,550.00
Badrul Yahaya	The effect of smoking on the stemness capabilities of lung stem cells in mice model of COPD	FRGS	Kementerian Pendidikan Malaysia	2019	3	157,700.00

Ghows Azzam/ Azalina Zainuddin	Elucidating the Molecular Pathway of THICAPPA and POET using *Drosophila melanogaster* Alzheimer's disease Models	TRGS	Kementerian Pengajian Tinggi	2020	3	364,400.00
Habibah A. Wahab	Elucidating the Mechanism of THICAPA and POET in Different Genetic Variants using Structural Bioinformatics	TRGS	Kementerian Pengajian Tinggi	2020	3	210,800.00
Eugene Ong	Unravelling the functions and targets of Leptospira interrogans virulence factors in a yeast model	FRGS	Kementerian Pengajian Tinggi	2020	3	146,300.00
					Total	**2,317,767.00**

3.3 Academic and Professional Membership

URICAS team members have received exclusive memberships to various national as well as international academic and professional bodies as recognition for their academic excellence. Table 5 shows the list of members invited to join said bodies.

Table 5: Membership in International Academic/ Professional Bodies/ Associations/ NGOs.

Principal Investigator	Academic body or Professional bodies	Status of membership	Start date	Level
Shukri Sulaiman	Advanced Center Computing and Communication, RIKEN	Project leader	4/4/2016	International
Shukri Sulaiman	Advanced Center Computing and Communication, RIKEN	Project leader	11/10/2017	International
Shukri Sulaiman	MAL-PAC	Member	1/2/2016	International
Shukri Sulaiman	Advanced Center Computing and Communication, RIKEN	Project leader	1/4/2018	International
Shukri Sulaiman	RIKEN	Member (Visiting Scientist)	1/4/2017	International
Shukri Sulaiman	RIKEN	Member (Visiting Scientist)	1/4/2018	International
Shukri Sulaiman	Advanced Center Computing and Communication, RIKEN	Project leader	3/4/2019	International
Sudesh Kumar	RIKEN	Consultant	1/4/2019	International
Sudesh Kumar	Malaysian Society of Microbiology	Executive member	1/1/2017	National
Sudesh Kumar	Academy of Sciences Malaysia	Fellow (FASc)	27/4/2019	National
Sudesh Kumar	Tropical Life Sciences Research	Editorial Board	1/1/2019	National
Sudesh Kumar	Malaysian Journal of Microbiology	Editor-in-Chief	1/1/2014	National
Eugene Ong	International Society of Infectious Diseases	Member	27/10/2017	International

Eugene Ong	American Society for Microbiology	Member	1/1/2019	International
Teh Aik Hong	American Chemical Society	Member	15/11/2017	International
Teh Aik Hong	Malaysian Nature Society	Member	19/8/2020	National
Teh Aik Hong	Persatuan Biokimia Dan Biologi Molekul Malaysia	Member	08/11/2017	National
Saidatulakmal Mohd	Persatuan Ekonomi Malaysia	Member	Life membership	National
Habibah A Wahab	Royal Society of Chemistry, UK	Fellow	2018	International
Habibah A Wahab	Lembaga Farmasi Malaysia	Member	2018	National
Habibah A Wahab	Malaysian Pharmaceutical Society	Member	2018	National
Habibah A Wahab	Malaysian Society of Pharmaceutical Technology	Member	2018	National
Habibah A Wahab	Pacific Rim Grid Application and Miiddleware Assembly	Steering Committee	2018	International
Habibah A Wahab	American Chemical Society	Member	2018	International

3.4 Awards

Members of URICAS teams have achieved academic excellence and were recognized for their contribution in research. Table 6 shows the list of awards conferred to URICAS PIs.

Table 6: Awards/stewardship conferred by National and International Academic and Professional bodies for research excellence.

Principal Investigator	Name of award	Conferring body	Level of excellence
Shukri Bin Sulaiman	Ahli Panel Penilai Buku	Pejabat Sekretariat Pemantau@KTP, Kementerian Pendidikan Tinggi	National
Shukri Bin Sulaiman	Ahli Panel Penilai ML-PAC	Program Advisory Committee for Materials and Life Science (ML-PAC) at RIKEN RI Beam Factory (RIBF)	International
Shukri Bin Sulaiman	Ahli Panel Penilai J-PARC MLF	Referee for Japan Proton Accelerator Research Complex (J-PARC) Materials and Life Science Experimental Facility (MLF) 2019B General Proposal	International
Sudesh Kumar	Top Research Scientist Malaysia	Akademi Sains Malaysia	National
Sudesh Kumar	Fellow of the Academy of Science Malaysia	Akademi Sains Malaysia	National
Sudesh Kumar	Ahli sidang Pengarang Tropical Life Research	Tropical Life Science Research	National
Sudesh Kumar	Consultant of RIKEN, Japan	RIKEN, Japan	International
Sudesh Kumar	External Moderator	RCSI & UCD Malaysia Campus	National
Sudesh Kumar	Executive Member	Malaysian Society of Microbiology	National
Sudesh Kumar	Editor-in-Chief	Malaysian Journal of Microbiology	International
Mohd Ghows Mohd Azzam	Young Investigator Award	Young Scientist Award	National
Saidatulakmal Mohd	Pension Experts Meeting	OECD Korea Policy Center	International
Saidatulakmal Mohd	Ahli Majlis Syuraa	Penang State Government	National

3.5 Patents and commercialization

The research conducted by URICAS are innovative and carry great impacts to the society. As such, three commercial patents were filed for the inventions of URICAS researchers as seen in Table 7. URICAS members currently hold two international patents and two national patents. In addition, a URICAS invention has also been registered with copyright rights as show in Table 8.

Table 7: Patents successfully filed by URICAS members.

Principal Investigator	Patent title	Patent description	Issuer country	Patent ID	Granted date	ID granted
Sudesh Kumar	Japanese Patent	Production Method for Polyhydroxyalkanoate Using Only Photosynthesis (Applicant: USM & RIKEN)	Japan	2015-551556	2019	6492011
Liong Min Tze	A wound healing-promoting protein, its encoding gene and uses thereof	Gene sequence of *Lactobacillus plantarum* responsible for the production of a bioactive protein with anti-staphylococcal and wound healing properties	Malaysia	PI 2016702784	2016	PI 2016702784
Liong Min Tze	Probiotic composition for treatment or prevention of high blood cholesterol	Composition of probiotic for treatment or prevention of high blood cholesterol	Malaysia	PI 2015702828	2015	PI 2015702828

Table 8: Copyrights obtained for URICAS inventions.

Principal Investigator	Category	Title of invention	Date registered	Registration Certificate Number
Shukri Bin Sulaiman	Copyright	Framework for the Study of Electron Transport in DNA	17/7/2020	LY2020002497
Teh Aik Hong	Copyright	Guided Manual Protein–Sugar Docking	10/9/2020	LY2020003698

3.6 Overall talent development

One of the main objectives in the establishment of URICAS was to nurture the new generation of scientists. URICAS successfully guided a total of 16 Masters students of which 15 students have graduated and 19 PhD students with 12 candidates completing their studies (Figure 7 and Table 9). In line with the principle of providing work opportunities to those who have graduated under URICAS, five post-doctorals (Table 10), 13 research officers and two research assistants (Table 11) were employed under URICAS. Figure 7 shows the overall talents cultivated by URICAS.

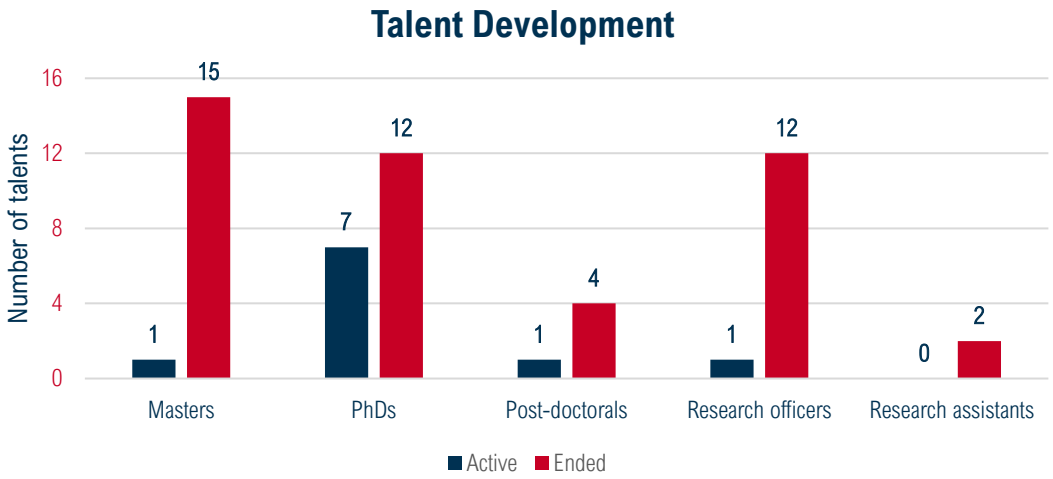


Figure 7: Overall talent development by URICAS.

Table 9: List of students supported by URICAS.

Name	Degree	Supervisor	Status
Melissa Qianyue Lian	MSc	Dr Teh Aik Hong	Active
Ang Shaik Ling	MSc	Prof. Sudesh Kumar	Ended
Lim Hui	MSc	Prof. Sudesh Kumar	Ended
Khor Ling Er	MSc	Prof. Gam Lay Harn	Ended
Teh Ying Hui	MSc	Prof. Gam Lay Harn	Ended
Kogaan A/L Anbalagan	MSc	Prof. Phua Kia Kien	Ended
Amy Lau Sie Yik	MSc	Prof. Liong Min Tze	Ended
Mohd. Hafis Bin Jaafar	MSc	Prof. Liong Min Tze	Ended
Ng You Kiat	MSc	Prof. Liong Min Tze	Ended
Siti Nuramira Binti Abu Bakar	MSc	Prof. Shukri Sulaiman	Ended
Koay Ley Teng	MSc	Dr Eugene Ong	Ended
Mandy Kwong Mun Yee	MSc	Dr Eugene Ong	Ended
Ong Tee Gee	MSc	Dr Eugene Ong	Ended
Yeap Kean Heng	MSc	Dr Teh Aik Hong	Ended
Sim Pei Fang	MSc	Dr Teh Aik Hong	Ended
Nurul Amirah	MSc	Prof. Habibah Wahab	Ended
Florence Tan	PhD	Dr Ghows Azzam	Ended
Azali Azlan	PhD	Dr Ghows Azzam	Active
Sim Xuan Yi	PhD	Prof. Gam Lay Harn	Active
Lew Lee Ching	PhD	Prof. Liong Min Tze	Ended

Hor Yan Yan	PhD	Prof. Liong Min Tze	Ended
Saidah Sakinah Bt Mohd Tajudin	PhD	Prof. Shukri Sulaiman	Ended
Harison Binti Rozak	PhD	Prof. Shukri Sulaiman	Active
Wan Nurfadhilah Zaharim	PhD	Prof. Shukri Sulaiman	Ended
Mira Syahfriena Binti Amir Rawa	PhD	Prof. Habibah Wahab	Ended
Erma Fatiha Muhammad	PhD	Prof. Habibah Wahab	Active
Kesevan	PhD	Prof. Habibah Wahab	Ended
Waeisa Waehamah	PhD	Dr Saidatulakmal Mohd	Ended
Mohd. Hadzril Bin Hassan	PhD	Dr Saidatulakmal Mohd	Ended
Lee Jee Whu	PhD	Dr Eugene Ong	Active
Tengku Yasmin Putri Binti Mohd. Yusop	PhD	Dr Teh Aik Hong	Ended
Nurulfatihah Mohd. Nasir	PhD	Prof. Shaharum Shamsuddin	Ended
Maisarah Ab. Samad	PhD	Prof. Shaharum Shamsuddin	Active
Shaheera Kamal	PhD	Prof. Shaharum Shamsuddin	Active
Jason Chin Khee Chian	PhD	Prof. Phua Kia Kien	Ended

Table 10:List of Postdoctoral fellows supported by URICAS.

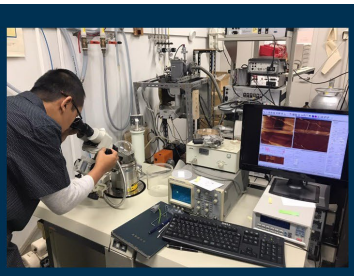
Name	Supervisor	Status
Dr Manoj Lakshmanan	Prof. Sudesh Kumar	Ended
Dr Lee Yan Fen	Prof. Gam Lay Harn	Ended
Dr Mardani Abdul Halim	Prof. Shaharum Shamsuddin	Ended
Dr Parisa Foroozandeh	Prof. Shaharum Shamsuddin	Ended
Dr Alex Foong Choon Pin	Dr Ghows Azzam	Ended

Table 11:Research officers and assistants supported by URICAS.

Name	Position	Status
Ferryn Ong Ting Fong	Research Officer	Ended
Nurul Aini Shamsuddin	Research Officer	Ended
Chin Chai Fung	Research Officer	Ended
Haania binti Zain Ali	Research Officer	Ended
Carlos Silvester	Research Officer	Ended
Shanmugapriya A/P Nathan Narayanaswamy	Research Officer	Ended
A.S.Navanithan	Research Officer	Ended
Nur Asmaa Athirah	Research Officer	Ended
Dr Jo-Ann Chuah	Research Officer	Ended
Lee Jee Whu	Research Officer	Ended
Lee Boon Kiat	Research Officer	Ended
Fiona Chung Yi Li	Research Officer	Ended
Florence Tan	Research Officer	Ended
Afiqah Azhar	Research Assistant	Ended
Bob Harris Norbert	Research Assistant	Ended

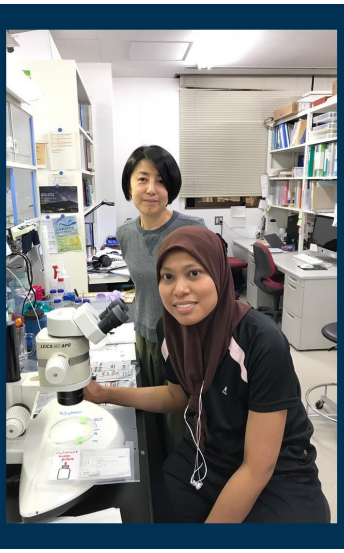
3.7 USM IPA Students at RIKEN

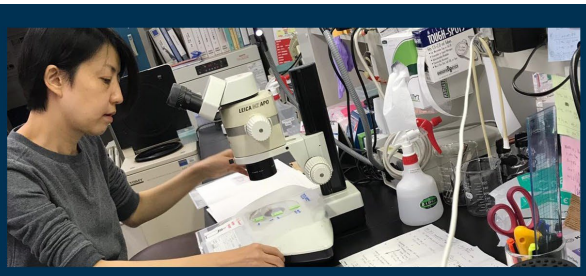
At RIKEN, students work alongside professional technicians and are mentored by established scientists in world-class facilities.



Mr Muhammad Hanif Che Lah (PhD Student), RIKEN Nishina Center for Accelerator-Based Science (Wako)

PICTURES: Prof. Koichi Ichimura (Left) and Hanif (Center) doing measurements on single stranded molecules in nanometer scales. (Right): Prof. Koichi Ichimura and Hanif in the Laboratory.



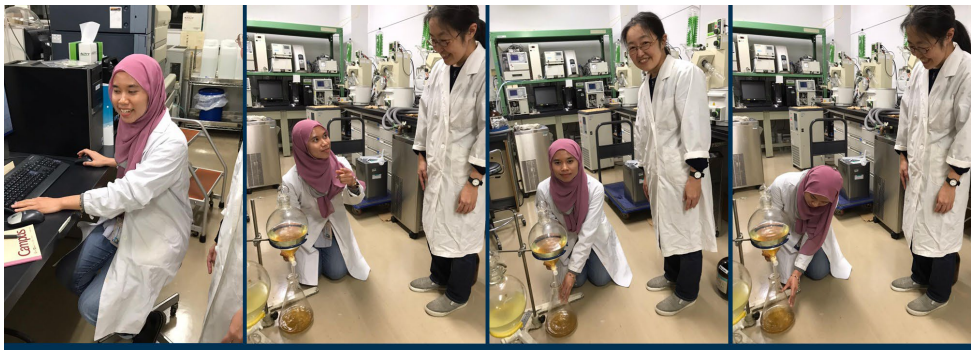


Ms Nor Shaheera Binti Mohamad Kamal (PhD Student), RIKEN Center for Biosystems Dynamics Research (Kobe)

PICTURE (Left): Shaheera (seated) performing experiments with a technical staff in JAPAN, Eriko Kajikawa (standing)

Ms Harison Binti Rozak (PhD Student), RIKEN Nishina Center for Accelerator-Based Science (Wako)

PICTURE : Harison (Center) with Dr. Isao Watanabe (Left) and Prof. Koichi Ichimura (Right) in the Laboratory

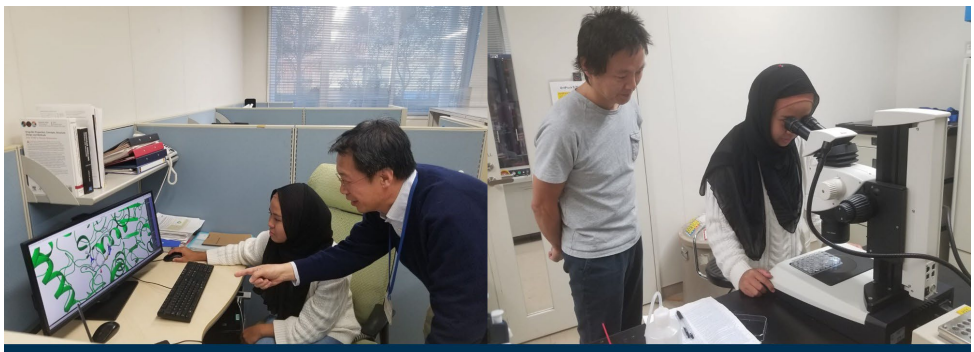


Ms Mira Syahfriena Binti Amir Rawa (PhD Student), RIKEN Center for Sustainable Resource Science (Wako)

PICTURES : (Far Left) Erma performing LC/MS analysis of sample to search for metabolites. (Left to Right) Erma performing solvent-solvent partitioning for metabolite isolation from fungi broth with a technical staff in JAPAN (standing).

Ms Maisarah Binti Ab Samad (PhD Student), RIKEN BioResource Center (Tsukuba)

PICTURES: Maisarah having a research meeting with Dr. Kuniya Abe (Principal Investigator) and Dr. Sugimoto Michihiko (Senior Postdoctoral fellow)



Ms Erma Fatiha Binti Muhammad (PhD Student), RIKEN Center for Life Science Technologies (Yokohama)

PICTURES: (Left) Erma with her Principal Investigator at RIKEN, Prof. Kam Zhang. (Right) Erma looking at crystal structure of proteins at the XRD Laboratory with a scientist in JAPAN, Dr. Ihara.

4.0 URICAS Activities

Throughout the 5 years , URICAS has actively organized various activities both for the advancement of its members as well as the betterment of the community. Table 12 shows the list of major activities throughout the 5 years. Detailed description of each year's activities will be expanded below.

Table 12:List of major URICAS activities 2015- 2021.

Year 2015		
Date	**Activity**	**Venue**
20 Feb	Signing of the URICAS MoU	RIKEN, Japan
Year 2016		
Date	**Activity**	**Venue**
23 Feb	URICAS Annual Meeting 2016	RIKEN, Japan
18 May	Dr Kuniya Abe's visit and seminar	INFORMM Auditorium, USM Main Campus
24 Aug	Seminar Assoc. Prof. Dr Ajioka and Dr Yoong Li-Foong, from RIKEN	INFORMM Auditorium, USM Main Campus
26 Aug	Prof. Dr Toru Takumi's visit and seminar	INFORMM Auditorium, USM Main Campus
Year 2017		
Date	**Activity**	**Venue**
27-28 Feb	URICAS Symposium 2017	INFORMM Auditorium, USM Main Campus
23 Nov	Visit and talk by Prof. William James Pro VC from Oxford	INFORMM Auditorium, USM Main Campus
Year 2018		
Date	**Activity**	**Venue**
1-2 Feb	URICAS Symposium 2018 in RIKEN	RIKEN, Japan
8 Feb	Visit to Silver Jubilee Old Folks home	Jalan Sungai Dua, Penang
	Appointment of Prof. Sudesh as a RIKEN Consultant	International Affairs Section, RIKEN Wako Branch
26-29 March	Turning Big data into small data	INFORMM Auditorium, USM Main Campus
22 May	Visit to Pusat Penjagaan Warga Emas, Darul Hanan	Kepala Batas, Penang
12 July	LRGS proposal workshop (USM-UKM-UPM)	Pusat Pengajian Sains Kajihayat, USM Main Campus
16 Nov	URICAS Student Research Progress Presentation November 2018	INFORMM Auditorium, USM Main Campus

Year 2019		
Date	**Activity**	**Venue**
21 Jan	Visit to PERKESO's Rehab Centre	Rehabilitasi Tun Abdul Razak, Melaka
4 March	Dr Todd Taylor's Workshop	Pusat Pengajian Sains Kajihayat, USM Main Campus
5 March	URICAS Symposium 2019	INFORMM Auditorium, USM Main Campus
7– 8 March	International Conference on Aging 2019	Eastin Hotel, Penang
16 April	Workshop on Physics of AGEING by Prof. Watanabe & Prof. Shukri	USM Health Campus
3 April	Manuscript Writing Workshop for URICAS Youngsters	Pusat Pengajian Sains Kajihayat, USM Main Campus
18 June	URICAS SWOT Analysis Workshop	INFORMM Auditorium, USM Main Campus
27 June	Meeting with HomeMedicare at IPPT	ARC, IPPT, USM Kepala Batas
16-17 July	Principle Component of Analysis	School of Pharmaceutical Sciences, USM Main Campus
8 Aug	Postdoctoral Fellow Colloquium	Conference room, TORAY Building, USM Main Campus
25-26 Nov	URICAS Workshop in RIKEN Singapore	RIKEN Representative Office, Singapore
Year 2020		
Date	**Activity**	**Venue**
3 Feb	Meeting with the Vice-Chancellor (USM) to discuss URICAS issues	Chancellory, USM
25 Feb	Meeting with Penang state executive councillor, YB Phee Boon Poh	Komtar, Georgetown
28 Feb	Meeting with the representatives of Pusat Aktiviti Warga Emas (PAWE), Balik Pulau	PAWE, Balik Pulau
May to Nov	Webinar for the elderlies	WebEx and Facebook Live
10 Sep	Anti-Fall Workshop	USM Kubang Kerian
27-28 Sept	Senior Technology Workshop	Kompleks Pentadbiran Kampus Kesihatan, USM Kelantan
Year 2021		
Date	**Activity**	**Venue**
4 Feb	URICAS Annual Meeting 2021	WebEx

4.1 Activities in 2015

4.1.1 Signing of URICAS MoU between USM and RIKEN

Taking place on the 20th of February 2015, this auspicious event signified the birth of URICAS and commemorated 20 years of collaboration between USM and RIKEN. A memorandum of understanding was signed by USM Vice-Chancellor, Prof. Dato' Dr Omar Osman and RIKEN President, Prof. Dr Ryoji Noyori (Figure 8).

Figure 8: USM Vice-Chancellor, Prof. Dato' Dr Omar Osman and RIKEN President, Prof. Dr Ryoji Noyori at the signing ceremony for URICAS in 2015.

4.2 Activities in 2016

4.2.1 URICAS Annual Meeting 2016

Members of URICAS gathered at RIKEN, Wako campus for the URICAS Annual Meeting 2016 on the 23rd of February 2016 (Figure 9). The main focus of the meeting was to discuss on the progress and future direction of the projects. The meeting was attended by USM Vice-Chancellor, Prof. Dato' Dr Omar Osman and RIKEN President, Prof. Dr Hiroshi Matsumoto (Figure 10).

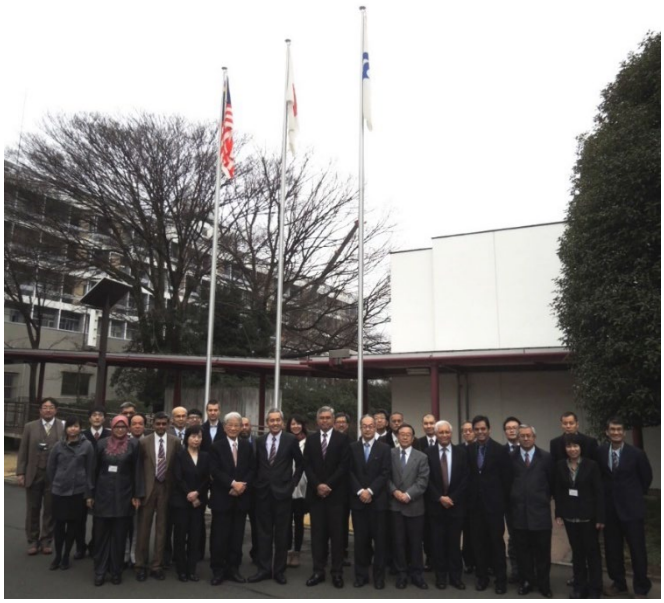


Figure 9: Members of URICAS in front of the Malaysia, Japan, and RIKEN flags.

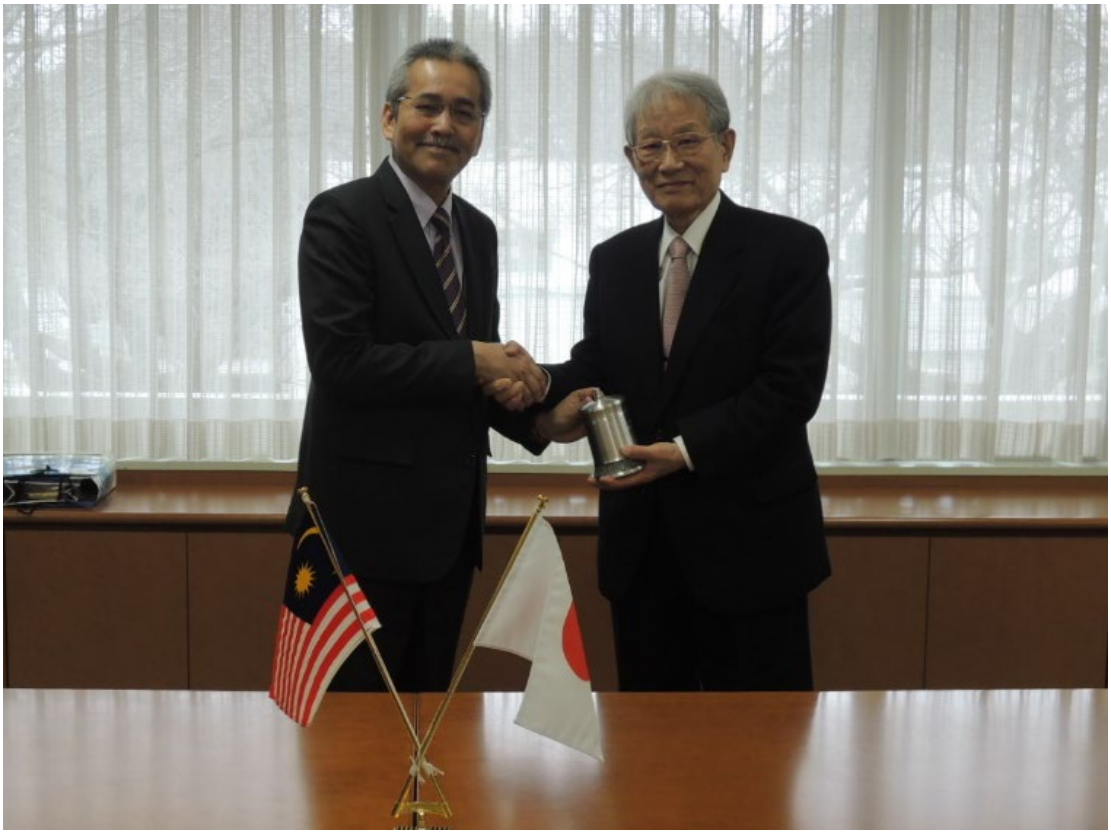


Figure 10: USM Vice-Chancellor, Prof. Dato' Dr Omar Osman and RIKEN President, Prof. Dr Hiroshi Matsumoto at the URICAS Annual Meeting 2016.

4.2.2 Dr Kuniya Abe's visit and seminar

On the 18th of May 2016, Dr Kuniya Abe was invited to give two talks at INFORMM Auditorium, USM Main Campus (Figure 11). This seminar is part

of a series of scientific seminars planned for the month of May at INFORMM, USM.

Dr Kuniya Abe's first talk entitled "An Introduction to RIKEN BioResource Center (BRC)" where he presented the BRC and discussed on how researchers can access the collection of bioresources at BRC for experiments. His second talk title "Robust induction of primed pluripotency in mammals: Wnt inhibition is critical for derivation and maintenance of mouse epiblast stem cells" whereby Dr Kuniya Abe and his team have devised a simple yet highly efficient protocol for EpiSC derivation and maintenance of homogenous, high-quality EpiSCs using small molecule inhibitor of Wnt signaling.

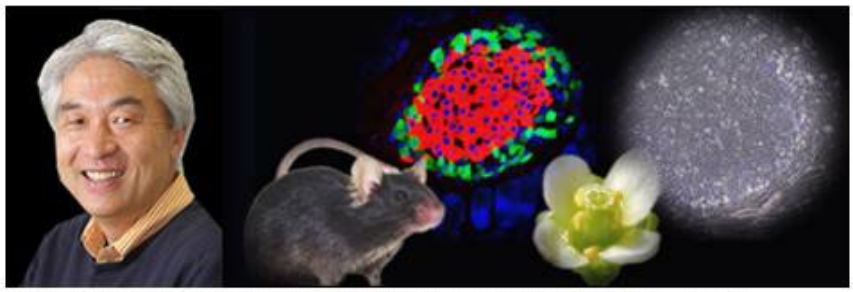


Figure 11: Image of Dr Kuniya Abe included in the poster for the May series of scientific seminars at INFORMM, USM.

4.2.3 Seminar by Assoc. Prof. Dr Ajioka and Dr Yoong Li-Foong

URICAS invited visiting scientists from Japan, Dr Li-Foong Yoong a Research Scientist at the Laboratory for Genetic Control of Neuronal Architecture at RIKEN Brain Science Institute and Assoc. Prof. Dr Itsuki Ajioka from the Center for Brain Integration Research at Tokyo Medical and Dental University to give lectures at INFORMM, USM on the 24th of August 2016.

Dr Li-Foong's talk, "How do neurons build their complex dendrite arbors?" discussed on her recent work of studying complex dendrite formation using a novel non-invasive, *in vivo* time-lapse microscopy approach. On the other hand, Dr Itsuki Ajioka introduced his recent finding on injured brain regeneration in his speech titled "Cell-cycle and Biomaterial Engineering for Injured Brain Regeneration" (Figure 12).

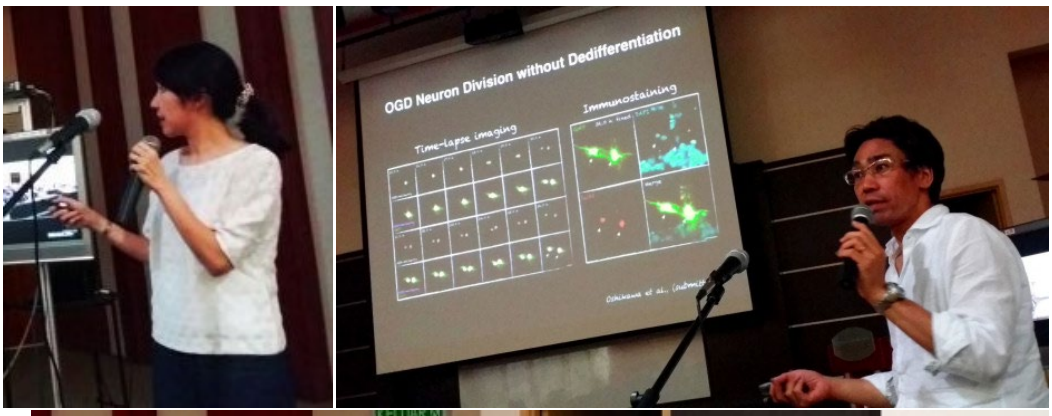


Figure 12: Poster to promote the seminar by Assoc. Prof. Dr Ajioka and Dr Yoong Li-Foong. Dr Yoong and Dr Ajioka during presentations. URICAS members with the speakers.

4.2.4 Seminar by Prof. Dr Toru Takumi

Prof. Toru Takumi gave a seminar at INFORMM Auditorium on the 26th of August 2016. His visit to USM was hosted by Prof. Liong Min Tze. In his talk "Mouse Model for Autism Spectrum Disorder: Towards understanding the pathophysiology," he showed his analyses on mice towards understanding the pathophysiology of autism spectrum disorder (Figure 13).

Figure 13: Poster to promote the seminar by Prof. Dr Toru Takumi.

4.3 Activities in 2017

4.3.1 URICAS Symposium 2017

The first URICAS symposium was organized and held in INFORMM, USM on the 27th to the 28th of February 2017. The main objective of the symposium was to foster deeper connections between USM and RIKEN counterparts within the URICAS teams as well as to gauge the teams' progress. The symposium was officiated by USM Vice Chancellor, Datuk Professor Dr Asma Ismail. At this symposium, 23 researchers from RIKEN and USM presented their research works, and USM students also participated by briefing and poster presentations of their projects (Figure 14).

Figure 14: Banner of the URICAS Symposium 2017. URICAS Youngsters at the URICAS Symposium 2017.

4.3.2 Talk by Professor William James

In November 2017, URICAS invited Prof. William James, the previous Pro Vice-Chancellor for Planning and Resource Allocation for the University of Oxford for a scientific seminar at INFORMM, USM (Figure 15 and 16). Prior to his seminar, Prof. William James had a special lecture with undergraduate students at DK SK1. During the afternoon session, Prof. William James discussed on two topics titled “Stem cell-based models for studying neuroinflammation and neurodegeration” and “Infectious disease” in Dewan Persidangan Universiti (DPU) (Figure 17). A discussion between Prof. William James and URICAS members were also conducted the next day at Chancellory II.

Figure 15: Promotional poster for Prof. William James' Scientific Talk.

Figure 16: Prof. William James and attendees at the Scientific Seminar at INFORMM.

Figure 17: Prof. William James and attendees at the discussion session in DPU.

4.4 Activities in 2018

4.4.1 The RIKEN-USM Workshop for URICAS 2018

The third URICAS meeting titled RIKEN-USM Workshop for URICAS was held from the 1st to the 2nd of February 2018 at RIKEN, Wako Japan. A series of presentations by USM and RIKEN principal investigators were held at the Suzuki Umetaro Hall. The annual meeting was conducted to update the teams' progress as well as to show the development of URICAS IPA students in RIKEN (Figure 18).

Figure 18: Promotional poster for the RIKEN-USM Workshop for URICAS. URICAS PIs and URICAS Youngsters during the RIKEN-USM Workshop for URICAS.

The third URICAS meeting titled RIKEN-USM Workshop for URICAS was held from the 1st to the 2nd of February 2018 at RIKEN, Wako Japan. A series of presentations by USM and RIKEN principal investigators were held at the Suzuki Umetaro Hall. The annual meeting was conducted to update the teams' progress as well as to show the development of URICAS IPA students in RIKEN.

At this meeting, USM management (Prof. Datuk Asma Ismail, Prof. Dato Professor Dato' Ir. Dr. Abdul Rahman Mohamed, Prof. Dr Lee Keat Teong) and Prof. K. Sudesh Kumar also had a top level meeting with RIKEN management (Prof. Dr Hiroshi Matsumoto anad Dr Hiroshi Ohno) to strengthen the USM-RIKEN collaborations (Figure 19).

Figure 19: Discussions between USM and RIKEN top managements during the 2018 meeting.

4.4.2 Visit to Silver Jubilee Old Folks home

As part of URICAS' mission to aid the aging society, URICAS organized a visit to the Silver Jubilee Old Folks Home at Sungai Ara, Penang on the 8th of February 2018. The visit was to perform communal work by helping caretakers spring clean areas of the Home as well as to bring a little cheer to the residents of the Home (Figure 20).

Figure 20: URICAS members and caretakers of the Silver Jubilee Old Folks Home

4.4.3 Visit by Dr Todd Taylor

Dr Todd Taylor visited USM, Penang and gave a workshop on the 28th of March 2018 in INFORMM. The workshop "Turning Big Data into Small Data Through Crowdsourced Curation: Integrating All Types of Medical and Scientific Knowledge" took a hands-on approach where Dr Todd showed attendees how to use the iCLiKVAL (iclikval.riken.jp), a web-based tool that uses the power of crowdsourcing to accumulate annotation information for all scientific media found online (Figure 21).

Figure 21: Left: Dr Todd giving his workshop. Right: Prof. Shaharum presenting Dr Todd a token of appreciation.

4.4.4 Visit to Pusat Penjagaan Warga Emas, Darul Hanan

As part of the community service activities planned by URICAS, members of URICAS visited the Pusat Penjagaan Warga Emas, Darul Hanan at Kepala Batas, Penang. URICAS members broke fast for Ramadan and enjoyed dinner with residents of the Pusat Penjagaan. A donation of RM1,100 was also made to the Pusat Penjagaan (Figure 22).

Figure 22: Dr Ghows and Prof. Nazalan talking to residents of Pusat Penjagaan Warga Emas, Darul Hanan. Breaking fast with the residents.

4.4.5 LRGS proposal workshop (USM-UKM-UPM)

On 12th July 2018, a joint workshop was held between three prestigious Malaysian universities: USM, Universiti Kebangsaan Malaysia (UKM) and Universiti Putra Malaysia (UPM). UPM was represented by Prof. Mayda Ir. Dr Siti Anom from Institut Penyelidikan Penuaan Malaysia, UPM while UKM was represented by Prof. Suzana Makpol and Prof. Emiratus Dato' Wan Zurinah Wan Ngah, both from the Faculty of Medicine, UKM. The purpose of this workshop was conducted as a series of brainstorming sessions in preparation for the Long-term Research Grant Scheme (LRGS) proposal on issues related to aging in Malaysia. This workshop was a platform for discussion, exchange of ideas, perspectives, experience, and dissemination of knowledge among students and senior researchers from the National Institute of Gerentology (MyAgeing UPM), UKM and USM (Figure 23).

Figure 23: URICAS members with UKM and UPM collaborators.

4.4.6 URICAS Student Research Progress Presentation November 2018

As the year closes in 2018, URICAS Youngsters presented their final progress report for the year. Eleven URICAS Youngsters reported their findings and were evaluated. The purpose of this was not only to gauge the development of the Youngsters but also to encourage and advice Youngsters on their projects (Figure 24).

Figure 24: URICAS Youngsters and URICAS PIs during the Research Progress Presentation.

4.5 Activities in 2019

4.5.1 Visits to PERKESO's Rehab Centre, Melaka (Pusat Rehabilitasi Tun Abdul Razak)

URICAS coordinator, Prof. Shaharum Shamsuddin visited PERKESO's Rehab Centre in Melaka on the 21st of January 2019. He was joined by Deputy Director HUSM and Rehab Medical Consultant.

4.5.2 Dr Todd Taylor's Workshop

Dr Todd Taylor was invited to conduct a workshop in the School of Biological Sciences, USM on the 4th of March 2019. His workshop titled "iCLiKVAL v2: Biocuration of online scientific media through the power of crowdsourcing and controlled vocabularies" was a continuation of his 2018 workshop. Similar to his previous workshop in USM, his 2019 workshop was a hands-on experience where he taught attendees to use the iCLiKVAL v2 (Figure 25).

Figure 25: Dr Todd Taylor and attendees of the workshop.

4.5.3 URICAS Symposium 2019

As the fourth annual URICAS meeting, the URICAS Symposium 2019 took place on the 5th of March 2019 in INFORMM Auditorium, USM. The focus of this forum was to discuss on research needs, exchange of information and ideas between URICAS members. This was also an opportunity for the URICAS Youngsters to hone their presentation skills with their one-minute presentation reports. The symposium was officiated by USM Research & Innovation Deputy Vice-Chancellor, Prof. Ir. Dr Abdul Rahman Mohamed. In addition (Figure 26), the signing ceremony of IPA by RIKEN Executive Director, Prof. Motoko Kotani & USM Vice Chancellor, Professor Datuk Dr Asma Ismail successfully commenced at the symposium, signifying the continuing relationship between USM and RIKEN (Figure 27).

Figure 26: URICAS members with Prof. Ir. Dr Abdul Rahman Mohamed at the URICAS Symposium 2019.

Figure 27: The IPA agreement signing ceremony. From left to right: Dr Hiroshi Ohno, Dr Motoko Kotani, Professor Datuk Dr Asma Ismail and Prof. Shaharum Shamsuddin.

4.5.4 International Conference on Aging 2019

URICAS organized an international conference on March 7th to 8th , 2019 in conjunction with USM's 50th anniversary. Assoc. Prof. Dr Badrul Hisham Yahaya took the helm as the chairperson for the conference committee and was co-chaired by Assoc. Prof. Dr Saidatulakmal Mohd. They received advised from Prof. Dr Shaharum Shamsuddin. USM's Vice Chancellor, Y.Bhg Prof. Datuk Dr Asma Ismail was the patron of the conference. The

conference focused on the tagline “ageing with dignity in a technological society.” It covered topics from fundamental life science to social issues affecting our daily lives. The conference included a diverse line-up of keynote and invited speakers including Prof. Robbyn Wacker from St. Cloud State University, Prof. Karl J. Neeser from Chulalongkorn University Bangkok, Prof. Dr Mukul G. Asher from National University of Singapore, Prof. Dato’ Dr Tengku Aizan Hamid from Universiti Putra Malaysia, Prof. Datuk Dr Wan Zurinah Wan Ngah from Universiti Kebangsaan Malaysia and Dr Achim D. Schmillen, Senior Economist from The World Bank.

The conference was officiated by YAB Tuan Chow Kon Yeow ,Chief Minister of Penang (Figure 28). In conjunction with the oral and poster presentation competitions, posters by contestants were displayed to be judged and sessions of oral presentations were conducted throughout the two-day event. On the second day, a forum consisting of panel of experts in aging was held. The panellist included Prof. Dato’ Dr Jafri Malin, Dr Carol Yip, Mdm Uta Dietrich and Dr Thomas Khor with Assoc. Prof. Dr Loke Yiing Jia as the moderator. Assoc. Prof. Dr Badrul Hisham Yahaya and Assoc. Prof. Dr Saidatulakmal Mohd gave their closing speeches and concluded the ceremony. This organisation and smooth running of the event was made possible by the contributions of all URICAS members, especially the students (Figure 29).

Figure 28: The Document Exchange Ceremony for the USM-RIKEN Collaboration.

Figure 29: Committee members of the ICA 2019.

4.5.5 Manuscript Writing Workshop for URICAS Youngsters

On 3rd April 2019, a URICAS Manuscript Writing workshop was held in School of Biological Sciences, Universiti Sains Malaysia. The objective of this workshop is to assist postgraduate students under the URICAS project on how to write manuscript research effectively (Figure 30). The facilitators for this workshop were Assoc. Prof. Dr Saiful and Assoc. Prof. Dr Sasidharan.

Figure 30: Assoc. Prof. Dr Saiful and Assoc. Prof. Dr Sasidharan with attendees at the URICAS Writing workshop.

4.5.6 Workshop on Physics of AGEING

A physics-themed workshop was organized and held at USM Health Campus. Facilitated by Prof. Shukri Sulaiman and Dr Isao Watanabe, the workshop aimed to show how physics was affected by ageing and how it helps with ageing through deeper understanding of the field (Figure 31). The workshop intersects the area of fundamental physics and medical physics.

Figure 31: Dr Isao Watanabe (top left) and Prof. Shukri Sulaiman (top right) presenting during the workshop. Bottom pic: Dr Isao Watanabe and Prof. Shukri Sulaiman along with Prof. Shaharum Shamsuddin and Prof. Dr Jafri Malin Abdullah from USM, Health Campus.

4.5.7 URICAS SWOT Analysis Workshop

On 18th June 2019, SWOT Analysis Workshop was held in Seminar Room 1 & 2 at Institute for Research in Molecular Medicine (INFORMM), Universiti Sains Malaysia. The objective of the workshop was to provide space for brainstorming sessions to set direction for URICAS after 2020, as well as to identify the weakness and advantage of each principal investigators (PI) in URICAS project (Figure 32). The workshop was attended by all the PIs and postdoctoral fellows of URICAS. On the same day, Jamuan Hari Raya Aidilfitri URICAS was also held in the Club House of INFORMM, Universiti Sains Malaysia. The event was also to celebrate the gratitude of the successful launch of the International Conference on Aging (ICA) 2019. Later in the afternoon, the outcome of the SWOT analysis was discussed, and the full report was successfully completed. The report was important to determine the future direction of URICAS Project.

Figure 32: URICAS PIs and post-doctoral fellows at the SWOT Analysis Workshop.

4.5.8 Meeting with HomeMedicare

A meeting was held between URICAS and HomeMedicare on the 27th of June 2019 at Institut Perubatan & Pergigian Termaju (IPPT), USM Kepala Batas (Figure 33). The meeting aimed to discuss on solving the problem with ageing problem in Malaysia and the possible collaboration with HomeMedicare. HomeMedicare was represented by Dr Thomas Kar and Dr Lee Li Ching.

Figure 33: URICAS and HomeMedicare members discussing during the meeting.

4.5.9 Dr Lee Yan Fen's Workshop

Dr Lee Yan Fen, a post-doctoral fellow of URICAS conducted a two-day workshop at Seminar Room DSAP, School of Pharmaceutical Sciences on the 16th and 17th of July 2019. Her workshop was titled "Principal Component Analysis (PCA) and Partial Least Square (PLS) analysis using SPSS and SIMCA: A Hands-on Approach" (Figure 34). The workshop explained ways to compress big data without losing useful data (dimensionality reduction), project a large data into simple plots that explain the major variance and ways to identify outliers from a given set of data.

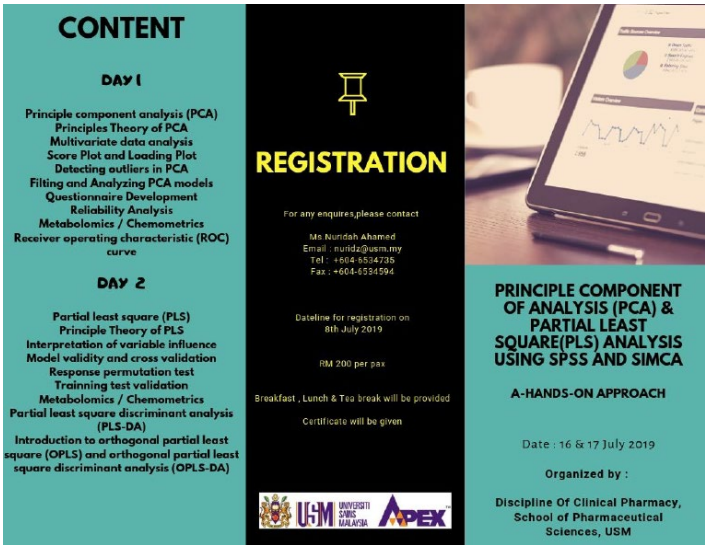


Figure 34: Brochure of the PCA and PLS workshop.

4.5.10 Postdoctoral Fellow Colloquium

On 8th August 2019, a short colloquium was organized for the URICAS post-doctoral fellows at the Conference room, TORAY Building, USM Main

Campus. The post-doctoral fellows presented their reports to be evaluated and to plan for URICAS fifth year (Figure 35).

Figure 35: URICAS post-doctoral fellow, Dr Manoj Lakshamanan presenting his report in front of URICAS PIs Prof. Shaharum Shamsuddin, Dr Ghows Azzam and Dr Teh Aik Hong.

4.5.11 URICAS Workshop in RIKEN Singapore

The 5th URICAS meeting was held on 25th – 26th November 2019 at RIKEN's Singapore Representative office in Singapore. The objective of the workshop was to facilitate brainstorming sessions and conduct critical discussions on the future of URICAS beyond the year 2020. The year 2020 will mark the fifth year of the URICAS programme and thus, provides a good impetus for self-examination and contemplation. The workshop was attended by the URICAS principal investigators (PIs) from Malaysia and Japan. Also invited to the Workshop were several independent reviewers from higher institutions of learning from Malaysia and Singapore (Figure 36).

The review committee was tasked with evaluating the achievements of URICAS since its inception in 2015 and the future viability of the programme for the next five years, 2020-2025. To acquaint the reviewers with the URICAS programme, they were provided with a whitepaper detailing its history and collaborative efforts. They were also given specific terms of references (TOR) as a guideline to perform the evaluation.

Fruitful discussions were had, and many impending issues were critically scrutinized by the PIs while being overlooked by the review committee. Towards the end of the workshops, the review committee gave an *ad hoc* summary of their findings and recommendations. An official report was prepared by the review committee and presented to the Vice-Chancellor of USM, Prof. Dr Faisal Rafiq Mahamd Adikan and the President of RIKEN, Dr Hiroshi Matsumoto on 14th January 2020.

Figure 36: URICAS members from USM and RIKEN during one of the workshops.

4.6 Activities in 2020

4.6.1 Meeting with the Penang State Government & Visit to the Pusat Aktiviti Warga Emas (PAWE), Balik Pulau

On 25th February 2020, URICAS principal investigators, Assoc. Prof. Dr Saidatul, Assoc. Prof. Dr Badrul, and Dr Eugene Ong had a meeting with a Penang state executive councillor, YB Phee Boon Poh at his office in Komtar, Georgetown. YB Phee Boon Poh is the chairperson of State Welfare, Caring Society and Environment Committee (Figure 37). The objective of the meeting was to initiate a collaborative effort between the two parties to help the elderly in Penang. The URICAS team presented a proposal report to YB Phee, which details the target location, proposed programmemes, and its benefits.

The proposal was received very positively by YB Phee and he has pledged to provide his support for the programmemes. He has acknowledged that the programmemes are much needed and will be greatly welcomed by the aged community. According to him, the proposed programmemes are also in alignment with the agendas of Penang Vision 2030, which heavily emphasizes the issues of family and community. He has also recommended that the URICAS team prepare a more comprehensive proposal report (long, short and mid-term programmemes) and define the terms of reference (TOR) so that it can be presented at the upcoming Penang State Exco meeting in March 2020.

On 28th February 2020, Assoc. Prof. Dr Saidatul and Dr Eugene travelled to Pusat Aktiviti Warga Emas (PAWE) at Balik Pulau to meet the representatives (Figure 38). The URICAS team was given a tour of the centre by the representatives. A discussion with them had provided more clues on the needs of the local elderly community, which can be incorporated into the new proposal report. Apart from that, the feedback gathered during the visit

could help the programmeme coordinators restructure their planned itinerary to increase the target audience's participation.

Figure 37: URICAS PIs discussing with YB Phee Boon Poh.

Figure 38: URICAS PIs discussing with representatives from Pusat Aktiviti Warga Emas (PAWE) at Balik Pulau.

4.6.2 Webinar Series for the Elderly

Throughout the year 2020, a series of webinars were conducted by the geriatric medicine experts at USM from the School of Medical Sciences in collaboration with URICAS. The main objective was to guide and provide solutions to the elderly on how to cope with the psychological stress and manage their existing medical conditions during the COVID-19 pandemic. At later stages, the scope of the webinar series was expanded to address other issues facing the elderly in everyday life. Experts from various disciplines in USM focusing on elderly issues were also invited to conduct the webinars (Table 12 and Figure 39).

Table 13:List of Webinars conducted.

Date	Title	Invited Speaker
7 May 2020	Tip-tip positif untuk Warga Emas di musim PKP	Prof. Madya Dr Asrenee Ab Razak
7 May 2020	Pengurusan Diabetes semasa pandemic di Bulan Ramadhan	Prof. Dr Azidah Abd Kadir
7 May 2020	Pengurusan ubat-ubatan Warga Emas di Bulan Puasa	Dr Siti Nurbaya Mohd Nawi
14 May 2020	Minda Ketara Sedar Warga Emas Berkasih Sayang dengan Diri Di Waktu Sukar	Prof. Madya Dr Asrenee Ab Razak
28 May 2020	Penuaan Aktif untuk Hari Tua Yang Lebih Ceria	Prof. Madya Dr Saidatulakmal Mohd
4 Jun 2020	Pencegahan daripada jatuh dalam kalangan warga emas	Dr Siti Nurbaya Mohd Nawi
18 Jun 2020	Warga Emas dan Kesunyian	Prof. Madya Dr Asrenee Ab Razak
16 Jul 2020	Amalan Pengubatan Selamat Buat warga Emas	Prof. Madya Dr Balamurugan Tangiisuran
23 Jul 2020	Penuaan Aktif dan Media Sosial	Dr Nik Norma Nik Hasan
3 Sep 2020	Isu dan Panduan Pemakanan Warga Emas	Prof. Dr Hamid Jan Bin Jan Mohamed
10 Sep 2020	Jenayah terhadap warga emas	Prof. Madya Dr Geshina Ayu Bte Mat Saat
24 Sep 2020	Fitness untuk Warga Emas	Dr Vina Tan Phei Sean
10 Oct 2020	Pokcik dah tua, bui lah ke hok muda pula	Dr Noor Haman Hamid
17 Oct 2020	Kesan COVID19 ke atas kesihatan mental warga emas	Dr Ahmad Shahril bin Ab Halim
7 Nov 2020	Kerapuhan tulang (osteoporosis) dalam kalangan warga emas Anggapan dan realiti	Dr Siti Nurbaya Mohd Nawi
23 Jul 2021	COVID-19 and the future of ageing: what are your options?	Prof. Madya Dr Saidatulakmal Mohd

Figure 39: Promotional posters for the webinar series conducted.

4.6.3 'Anti-Fall' Workshop

On the 10th of September 2020, with the assistance of Geriatrics Rehab MOH, the 'Anti-Fall' workshop was conducted to train all USM's Rehab staffs serving all campuses (Figure 40). This training was designed to provide a combination of strategies and effective ways to reduce falls among the elderly as well as the rehab medical treatment.

Figure 40: Attendees at the 'Anti-Fall' Workshop.

4.6.4 Bengkel Teknologi Senior

Bengkel Teknologi Senior, a project led by Dr Tan Yun Yi, was selected as one of the recipients of Star Golden Hearts 2020 Award (Figure 41). The workshop ran from the 27th to the 28th of September 2020. Bengkel Teknologi Senior aimed to bridge the digital literacy gap, at a time when the world relies on digital connection more than ever. The main goal was to increase the technological capacity, skills and competency of pre-retirees and retirees through workshop courses that were specifically developed for the target group of over 55 years old (Figure 42).

Figure 41: The workshop was led by Dr Tan Yun Yi (winner of the Star Golden Hearts Award 2020). Promotional poster for the workshop.

Figure 42: Dr Tan Yun Yi and attendees at the workshop.

4.7 Activities in 2021

4.7.1 URICAS 6th Annual Symposium

URICAS held their 6th Symposium on the 4th of February 2021. Due to current situations, the meeting was done in a virtual set-up via WebEx (Figure 43). The event was officiated by Yang Bahagia Prof. Dato Ir Dr Abdul Rahman Mohamed, Deputy Vice-Chancellor of USM. The meeting also introduced Dr Takashi Kawabe as the new director of the RIKEN Singapore office.

During the meeting, both RIKEN and USM delegates discussed on the past activities on URICAS and the current situation of both institutes as well as suggestions on 'The Way Forward'. The discussion was a fruitful one where many solutions were suggested. The event closed with speeches from Prof. Shaharum Shamsuddin, USM's URICAS Coordinator and Dr Todd Taylor, RIKEN's URICAS Coordinator.

In conjunction with this meeting, URICAS has organized a video competition specifically for URICAS Youngsters. Youngsters talk about their projects in 3-minute long videos. In addition, one of the main objectives of URICAS was to develop young research talents. Students selected for the prestigious IPA programme were assigned a research project at any of the 10 RIKEN campuses in Japan to work under the supervision of a RIKEN principle investigator. Since URICAS started in 2015, we had 11 (6 short-term) and (5 long-term) IPA students. For this event, our previous and current IPA students under URICAS have prepared short videos to show their experience in both RIKEN and Japan.

Figure 43: Promotional poster for the URICAS 6th Symposium (right) and the participants (left).

4.7.2 URICAS Webinar

A webinar was organized by URICAS on 27th December 2021. The participants were invited to join the webinar via Webex video conferencing. Dr Hiroshi Ohno from the RIKEN Center for Integrative Medical Sciences delivered the opening remarks at the webinar and the welcome address was given by the Deputy Vice-Chancellor, Academic & International of Universiti Sains Malaysia, Professor Dato' Dr Narimah Samat (Figure 44).

The first speaker, Dr Nobumoto Watanabe (Bioprobe Application Research Unit, RIKEN Center for Sustainable Resource Science) delivered a presentation entitled 'Screening of bioactive compounds – Perspectives of the usage of ROS Inducers for cancer therapy'. The second speaker, Professor Dr Habibah Binti A Wahab (School of Pharmaceutical Sciences, USM) delivered a presentation entitled 'Modelling natural product for drug discovery – How effective are the models ?'.

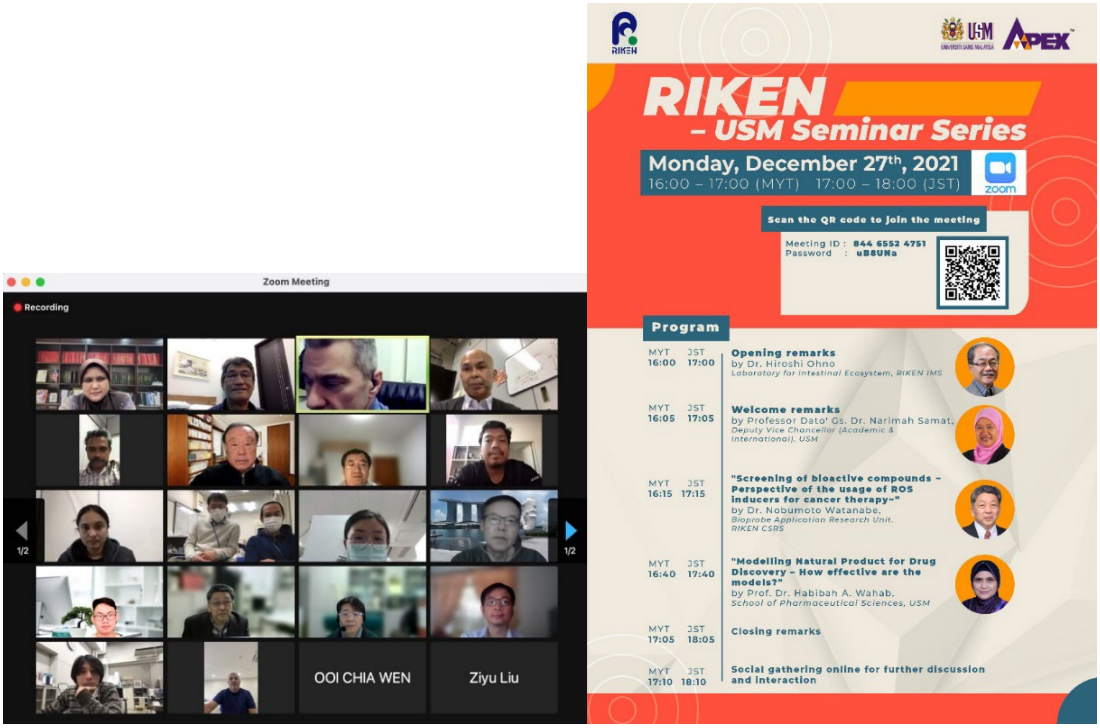


Figure 44: Promotional poster for the URICAS seminar (right) and the participants (left).

5.0 URICAS: The Way Forward Workshop (November 2019)

5.1 Review of the URICAS programme

A special joint meeting was held at RIKEN's Singapore Representative Office on the 25th – 26th November 2019 to discuss and set the course for the future direction of URICAS as the five-year programme was coming to an end in 2020 (however due to the COVID-19 pandemic, the programme was extended to 2021). External reviewers that were not a part of URICAS were invited to sit in and listen to research findings by all team leaders and moderate as well as review the programme since it started in 2015.

5.1.1 Review Board Members

- Professor Dr Yoshiaki Ito (National University of Singapore)
- Professor Dr Jun Li (National University of Singapore)
- Professor Dr Musalmah Mazlan (Universiti Teknologi MARA)
- Professor Dr Norazmi Mohd Nor (Universiti Sains Malaysia)

5.1.2 The Terms of Reference

The terms of reference of the review are,

- TOR1 Evaluate current URICAS organisation structure on USM and RIKEN sides based presented SWOT analyses
- TOR2 Evaluate whether URICAS has achieved its past objectives
- TOR3 Evaluate URICAS student training efforts and outcomes
- TOR4 Evaluate USM-RIKEN collaboration research/technology output
- TOR5 Evaluate inter/cross-disciplinary efforts within URICAS teams
- TOR6 Evaluate brain circulation and internationalisation efforts under URICAS
- TOR7 Evaluate the scientific appropriateness of the future strategic and organisational structure of URICAS
- TOR8 Recommendations concerning future scientific direction, improving networking and organisational structure

5.1.3 URICAS – SWOT Analysis – USM

Executive Summary

The SWOT analysis identified the **strong collaboration with Japan** and the **multidisciplinary research character of URICAS** as key strengths. On the contrary, areas currently exhibiting weaknesses are **future financial support** and **potential brain drain**.

Key opportunities arising from the URICAS collaboration are engagement in translational research and international collaboration with RIKEN scientists. URICAS continuation is threatened by an uncertainty of future financial support and limited scientific output.

Termination of the URICAS programme will have adverse effects on the selection and funding of future USM-IPA students, especially considering recent regulatory changes concerning USM-fellowships.

Goal

Improve academic/industrial collaboration between Japan and Malaysia (long term).

Vision

Advancing USM-RIKEN multidisciplinary collaboration through training and research.

Summary

The SWOT analysis from the USM perspecive is summarised in the following page (Table 13).

Table 14: SWOT analysis from the USM perspective.

Internal Factors	
Strengths	**Weaknesses**
• What we do well? • What unique resources can you draw on? • What do others see as your strengths?	• What could you improve? • Where do you have fewer resources than others? • What are others likely to see as weaknesses?
– Well-balanced researchers, Postdocs, and graduate students – Multidisciplinary research areas – Strong collaboration with Japan – Availability of internal funding from USM – Good research facilities – USM promotes gender equality – USM #1 of the 2018 GIR-Times Higher Education SDG ranking in Malaysia	– Office space and facilities – Human resources – Funding and Procedures – Research focus – Research deliverables
External Factors	
Opportunities	**Threats**
• What opportunities are open to you? • What trends could you take advantage of? • How can you turn your strengths into opportunities?	• What threats could harm you? • What is your competition doing? • What threats do your weaknesses expose you to?
– Request for office space / laboratories – IPA graduates recruited as Postdocs under URICAS – Clear expectations on outcome (deliverables) – Opportunity for PIs and young researchers to collaborate with world-class RIKEN scientists – Engage in translational research – External funding – Possibility of publication after three years in high impact journals	– Financial Support – Publications

5.1.4 URICAS – SWOT Analysis – RIKEN

Executive Summary

The SWOT analysis identified the **state-of-the-art research environment**, **involvement of a large number of RIKEN centers** and **interdisciplinary research culture** as key strengths. On the contrary, areas currently exhibiting weaknesses are **inter-team networking and communication**, **RIKEN-side URICAS organisational structure** and current **focus on ageing research**.

Key opportunities arising from the URICAS collaboration are **identification/recruitment of good short/long-term IPA students**, **support to establish post-IPA students at USM** and **nurture future Japan/Malaysia industrial and academic collaborations**. URICAS continuation is threatened by a **shift in RIKEN's strategic orientation**, a **narrow focus on one-on-one collaborations** and a **limited scientific output**.

In general, it is understood that termination of URICAS financial support will have adverse effects on the selection and funding of future USM-IPA students.

Goals

Expand basic and applied scientific knowledge and improve academic/industrial collaborations between Japan and Malaysia (long term).

Vision

To grow the RIKEN-USM research collaboration on basic science with a specific focus towards applied science. Within this framework, selected students from USM will receive special training at RIKEN focused on basic science and receive a chance to proceed with their research career at USM. Additionally, students involved in this collaboration will not only act as messengers of Japan in Malaysia in academia and industry, but also represent a valuable asset for Japanese industry due to their experience at RIKEN.

Summary

The SWOT analysis is summarised in the following page (Table 14).

Table 15: SWOT analysis from the RIKEN perspective.

Internal Factors	
Strengths	**Weaknesses**
• What we do well? • What unique resources can you draw on? • What do others see as your strengths?	• What could you improve? • Where do you have fewer resources than others? • What are others likely to see as weaknesses?
– long history and reliable collaboration – cutting edge, basic research – interdisciplinary research and research culture – involvement of many RIKEN centers – environment to nurture select post-IPA students at USM	– lack of RIKEN-side URICAS structure – low use of English at RIKEN – strong focus on ageing science – limited translational capabilities from basic to applied science – rigid one-on-one collaborations
External Factors	
Opportunities	**Threats**
• What opportunities are open to you? • What trends could you take advantage of? • How can you turn your strengths into opportunities?	• What threats could harm you? • What is your competition doing? • What threats do your weaknesses expose you to?
– short/long-term IPA students trained in RIKEN can continue at USM – sharpen direction and structure of RIKEN-side URICAS – RIKEN trained students promote Japan-Malaysia collaboration in academia and industry – reduce Japanese industries labour and skill shortage by attracting young Malaysian talents with RIKEN training	– unrelated RIKEN-Ageing project – RIKEN strategic orientation directed towards EU/US collaborations with narrow research focus – one-on-one collaboration setup impedes development of network and free scientific exchange – loss of financial support hampers selection of suitable IPA students – weak translational capability reduces visibility and funding opportunities

5.2 URICAS – Future Strategic Direction and Vision

During the past 5 years the strategic direction of URICAS was focused on Ageing Science. This focus supported the establishment of the Ageing Science Research Cluster at USM, which gained national and international visibility and recognition, as exemplified by the successful organisation of the 'International Conference on Ageing – ICA 2019' in Penang. As outlined in the RIKEN-SWOT analysis, the RIKEN teams have a need to readjust their focus to basic and advanced science.

To allow combination of the two strategic orientations of the involved institutes, URICAS will adopt the following strategic direction:

- RIKEN side: USM-RIKEN collaboration will focus on basic science and the development of advanced science and technology
- USM side: USM-RIKEN collaboration will extend joint scientific results as well as drive joint technology towards application with a focus on ageing science

A distinct feature of URICAS is the broad scientific background ranging from nuclear physics (muon research) over chemical biology to biomedical research of the involved teams. This diversity is highlighted in the involvement of 9 different Schools at USM and 7 Centers at RIKEN. To harvest this unique interdisciplinary character, network formation between URICAS members and teams will be promoted.

The adoption of the Sustainable Development Goals (SDG) in 2015 was a milestone to guide national and international economic and social development. Continuing the spirit of the 2015 signed USM-RIKEN agreement founding the URICAS programme which enshrined the mission to contribute to international society, including in Asia, URICAS will expand its strategic direction towards SDG. In this context URICAS will identify within the 5th URICAS Workshop framework the top three SDGs that URICAS will specifically address.

The joint mission of URICAS will be based on three pillars, discovery of novel bio(medicinal)resources from Malaysia, development of novel technologies and training of human resources. As example this includes, identification and characterisation of novel bio(medicinal)resource, such as bioplastic producing microorganism. Furthermore, the joint development of stem cell and organoid technology will not only provide improved biomedical tools, but also represents unique opportunities to train young scientist in cutting edge technologies. At the same time, joint progress in muon technology will provide a novel viewpoint on material characteristics of soft bio-matter. These cooperative achievements in basic and applied science will not only support the growth of Ageing science at USM, but also represent a significant contribution towards the SDGs.

5.3 URICAS – Future Objectives

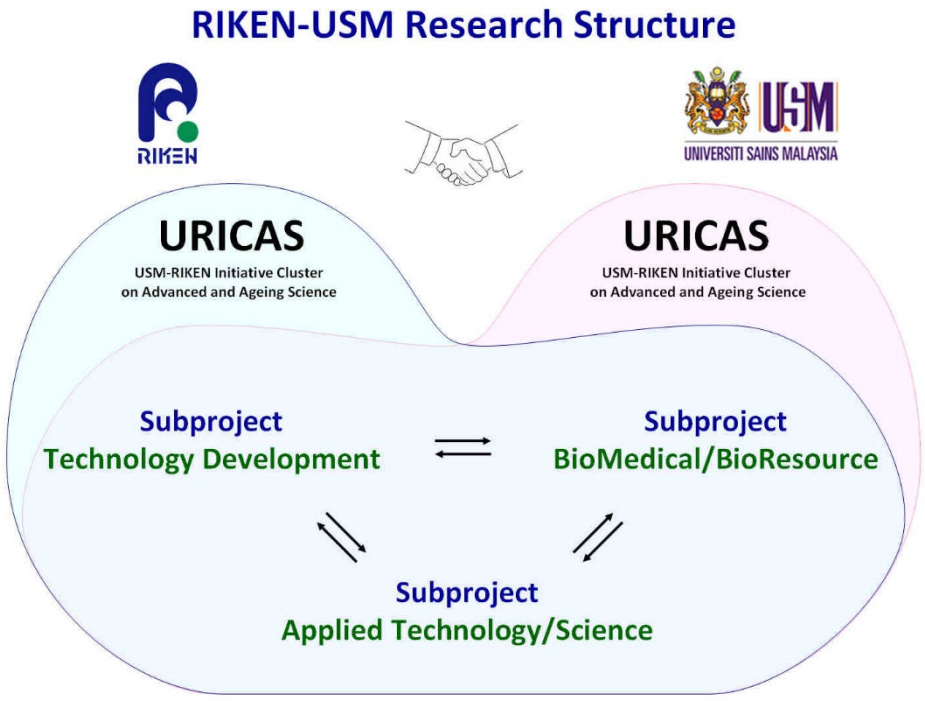
- Stimulate broader interdisciplinary collaboration between URICAS teams.
  - promote creation of research networks.
  - maintain already established one-on-one collaboration.
  - each URICAS member will join one of the three URICAS subprojects.
    - **Technology development**

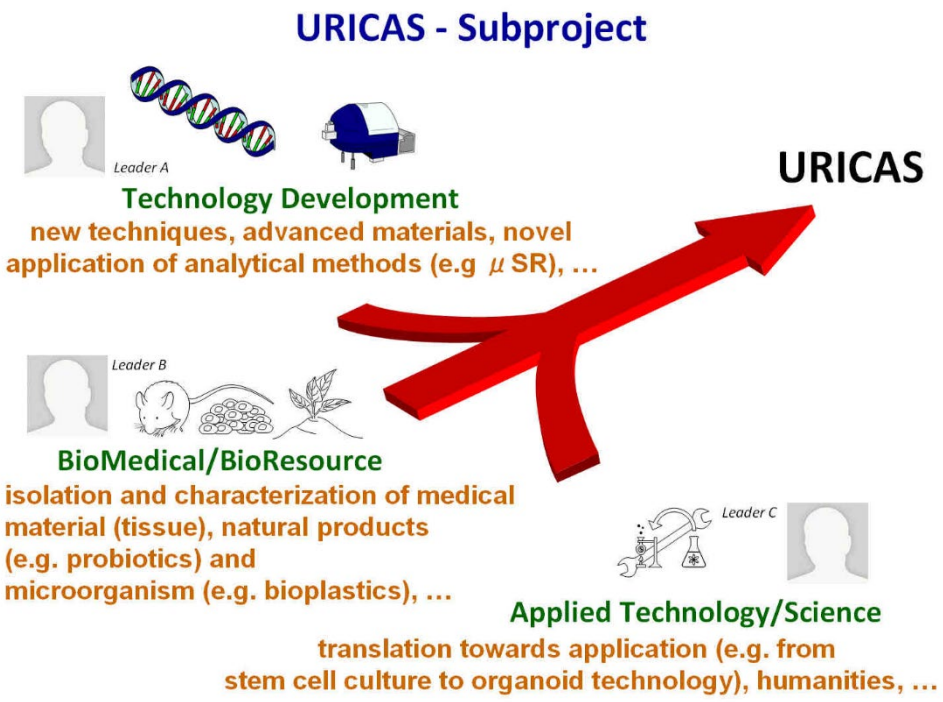
      new techniques to study advanced materials, novel application of analytical methods (e.g., μSR).
    - **BioMedical/BioResource**

      isolation and characterisation of biomedical material (e.g., tissue from animal experiments), natural products (e.g. probiotics) and microorganism (e.g. bioplastics).
    - **Applied technology/Science**

      translation towards application (e.g. from stem cell culture techniques to organoid technology).
  - each subproject does not need same number of participants.
  - each subproject will select a leader and co-leader.
  - each subproject will be encouraged to stimulate scientific exchange (e.g. via workshops) to promote joint research within and between subproject groups.
- Move research focus towards identification/characterisation/application of novel bio(medicinal) resources but maintain ageing science as a target direction at USM.
- Continue regular research exchange and promote wider RIKEN-USM collaborations.
  - continue annual URICAS meetings.
  - promote exchange with seminar series, e.g. RIKEN scientists (can also be non-URICAS members) give seminars at USM.
- foster post-IPA programme at RIKEN and USM - (early career support programme).
- promote research contributing to top URICAS – SDGs.

5.4 URICAS – Future Structure





END OF URICAS REPORT 2015-2021


UNIVERSITI SAINS MALAYSIA
APEX
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