UNIVERSITI SAINS MALAYSIA

MRP Bulletin 2020

Monthly Research Presentation

SCHOOL OF MEDICAL SCIENCES

Contents

"Butterflies are graceful & enchanting yet approachable. It can lead us to the sunny side of life..."

- MRP Team 2020 -

From Dean
School of Medical Sciences

Assalamualaikum & Salam Sejahtera.

May Allah s.w.t showers His countless blessing on all of us.

I would like to take this opportunity to thank Professor Dr. Rosline Hassan as a Deputy Dean (Research) and her team for organizing this MRP e-bulletin for the year 2020.

Due to Pandemic Covid-19, we have managed only 6 sessions of MRP this year, which I consider as very successful despite the challenges that we are facing.

I must mention that the quality of research and presentation is getting better and better for PPSP, Alhamdulillah. The team has selected various presentations ranging from fundamental research to clinical research. In the last MRP, we even invited our former PhD student who is currently our Postdoc to present her work. We had a very refreshing session.

Congratulations to the team and we pray that PPSP will fly further to produce higher impact research to the society.

Thank you.

Professor Dr. Shaiful Bahari Ismail
Dean
School of Medical Sciences
Universiti Sains Malaysia

"Be willing to be transformed.
Without change nothing
beautiful would happen"

- MRP Team 2020 -

From Deputy Dean Research & Innovation

Assalamualaikum warahmatullah & Salam Sejahtera

Dear Colleagues,

Alhamdulillah, year 2020 is coming to the end. Congratulation to Dr. Wan Faiziah Wan Abdul Rahman and committee members who have successfully conducted a new Norm of Monthly Research Presentation (MRP).

COVID-19 pandemic has placed a tremendous improvement in research delivery to the academician. The committee creativity through online research presentation can be accessed and shared by many participants, attendance beyond 100 would provide a positive research environment. A huge thanks and appreciation to all the experienced speakers who have committed their time and sharing invaluable piece of materials in this first edition MRP Bulletin. I am indebted to all who have contributed to the delivery of this very first publication and it is hoped that the bulletin will uplift the knowledge and research motivation.

Enjoy reading and May ALLAH bless us and grant our work with barakah.

Thank you,

Professor Dr. Rosline Hassan
Deputy Dean (Research & Innovation)
School of Medical Sciences
Universiti Sains Malaysia

"Research is about creating change."

- MRP Team 2020 -

from the desk of MRP

Chairperson

السَّلَامُ عَلَيْكُمْ وَرَحْمَةُ اللهِ وَبَرَكَاتُهُ

Salam Sejahtera

Alhamdulillah.

Special thanks to MRP advisor, Professor Dr Rosline Hassan, our deputy dean research & innovation for her guidance and trust in my team to execute the new norm MRP for this year. Now I would like to take this privilege to WELCOME everyone to the 1st edition of **MRP bulletin 2020:** ***Transforming ideas into reality***. This inaugural piece is a compilation of research synopses that assembled a diverse group of successful research and innovation throughout the year that absolutely able to inspire you.

We believed that every research has a story to tell and behind of every success has a route to share. We realized that sometimes all we need is a little inspiration to keep rolling. Therefore, by presenting this special piece with butterfly concept, hopefully would encourage us to change beautifully and inject some motivation in research and publication.

I would like to thank all the great speakers for their full commitment in delivering the talk and preparing the synopses, to the fantastic MRP team for their hard work, to the Research Committee for rotating in being an emcee and to our beloved Dean, Deputy Deans and all lecturers for being such an enthusiastic listeners with great support.

Thank you,

Dr. Wan Faiziah Wan Abdul Rahman
Chairperson
Monthly Research Presentation 2020
School of Medical Sciences
Universiti Sains Malaysia

"Just simply flies on like butterfly.....
Look back upon the caterpillar self
for sharing and motivation"

- wfwar 2020 -

MRP GOALS

To **introduce good researchers** in PPSP

To give **opportunity** for researcher **to share** their research & innovation

To **emphasize** on research with certain **grants award**

To **encourage** research **collaboration**

To **motivate** researcher to **publish** their research in **high impact journal**

"A burning desire is the starting point of all accomplishment"

- MRP Team 2020 -

MRP Bulletin 2020

12 RESEARCH SYNOPSES
SCHOOL OF MEDICAL SCIENCES

"It is never too late to transform ourselves"

- MRP Team 2020 -

Designing Impactful Project: From Lab to Community via Zucademic Model

Dr. Mohd Zulkifli Mustafa [zulkifli.mustafa@usm.my]
Department of Neuroscience, School of Medical Sciences
Universiti Sains Malaysia

Does academia in higher education institutions nowadays have a vision? Or it is merely a personal fight for living one's own legacy? or just being trapped in the conservative system and being tired holding on to the stagnant practices?

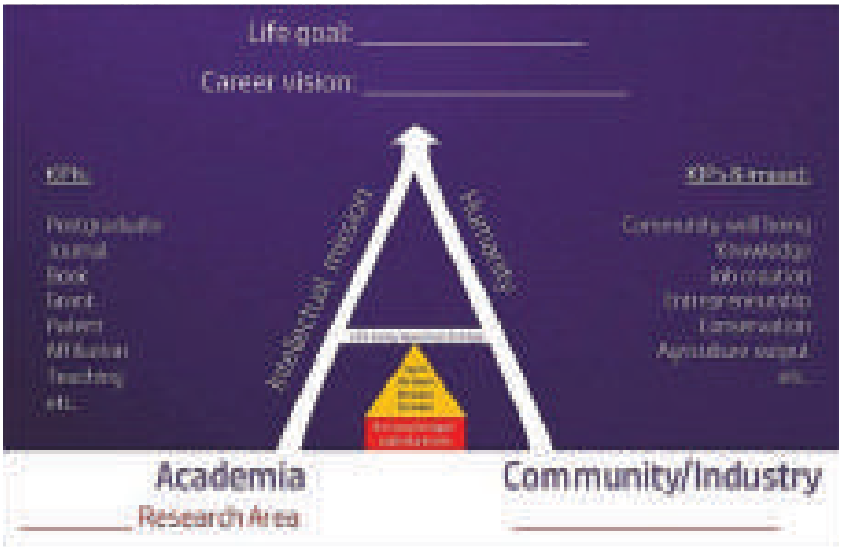
Today, higher education institutions are emphasized for global ranking through competency of high-impact research and publication. This comes with prerequisite Key Performance Index (KPI) of being a lecturer, mainly teaching, research works, student supervision, book writing, thesis evaluation and additional management activities. These tasks are further loaded by the need to develop products and commercialization. University has also been questioned for its contribution to the local community, hence the introduction of community engagement-based activities. The community engagement (CE) has now become a crucial platform for academia which serves as a new and effective way of developing, transmitting and applying knowledge. The main goal? To bring benefits to the public and to help tackle real-world problems.

Rather than asking what the university should do, I challenged myself with two big questions. One; what do I fight for in life? And two; where am I heading? And I discover that a clear vision could actually provide a holistic initiative to empower both university and community simultaneously. In a standard framework of Scholarship of Teaching and Learning (SoTL), the goal setting for an educator should start with contributing to educational mission. This is followed by advancing knowledge in the field, with and the engagement in educational community coming in last.

My personal experience has however, points in the different approach. CE should come first or together along with my academic career towards the vision. In this initiative, my path in intellectual mission was designed along with community empowerment path that I termed as my humanity mission towards achieving the vision and life goal. These two missions are connected via one lifelong learning bridge (LLB), forming an "A" metric known as Zucademic Model. Via LLB, CE is not a one-off project but a continuous academic process that becomes a medium for knowledge validation at community or industry groups. As an example, I wrote a module book (as tool to engage with community) and conducted beekeeping workshops to over 3000 participants. They constitute the "stingless beekeepers tribe" (target community) and act directly in producing high quality honey towards a vision to uphold Kelulut honey as a new commodity for country. Several spill-over impacts promote the activity to become a new agro-economic opportunity for rural development and transformation. The model facilitate me in designing impactful research project, secure grants and patents as well as achieving my Key Intangible Performance (KIP) for community wellbeing and ecology sustainability via bee conservation program.

It is truly a liberty when I realized that my credibility as a scholar is not merely for personal-expression, but more importantly, as a medium to serve the people whom I belong to. Don't confuse between our own legacies and the life objective of a scholar.

Figure 1: Zucademic Model to achieve KPI & KIP



Immunohistochemical Staining to Investigate Osteoclast-Specific Marker, Nuclear Factor of Activated T Cells 1 (NFATc1) in Giant Cell Tumour of The Bone (GCTB)

Dr. Muhamad Syahrul Fitri bin Zawawi [msf.zawawi@usm.my]
Department of Orthopaedic, School of Medical Sciences, Universiti Sains Malaysia

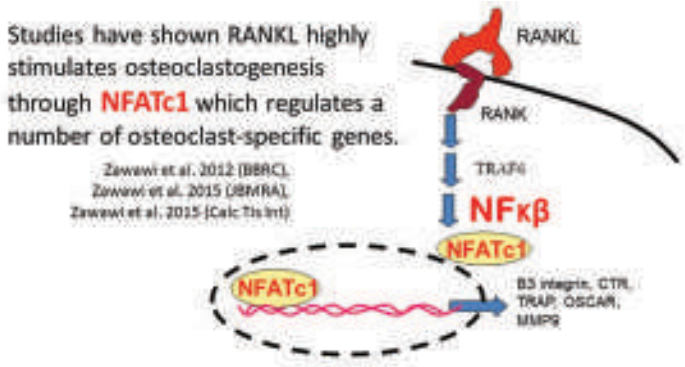
Osteoclastic bone resorption and osteolysis with tendency for local recurrence and pulmonary metastases are a common complication of stage III Campanacci giant cell tumour of the bone (GCTB) (1,2). Studies have shown receptor activator of nuclear factor κB ligand (RANKL) highly stimulates osteoclastogenesis through nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1 (NFATc1) which is involved in the regulation of a number of osteoclast-specific genes (3). Osteoclastogenesis is retarded in NFATc1 suppression and knocked-out embryonic stem cells *in vitro* (4). To our knowledge, the regulation of NFATc1 in osteoclastic resorption in GCTB has not been studied in stage III GCTB. We analyzed NFATc1 expression by immunohistochemistry technique in 31 consecutive cases of stage III GCTB to understand the clinico-pathological correlation.

This study involved 31 consecutive cases of stage III Campanacci giant cell tumour of bone (GCTB) operated and treated at Hospital Universiti Sains Malaysia from January 2004 to December 2017. Expression of NFATc1 was assessed using immuno-histochemical staining method in all representative archive tumour sections. Serial sections of 5μm was cut and stained by immuno-histochemical techniques. NFATc1 expression over nuclear area of tumor cells were examined and evaluated in three random microscopic fields using a standard light microscope at 40 x 100 magnification by two-blinded independent observers. Positivity for NFATc1 expression was assessed according to percentage of 1000 background cells using an image analysis software (Olympus - U-RFL-T Cell F). The highest score from three selected fields was taken for statistical analysis using SPSS version 25.0. Statistical analysis was carried out using independent *t*-test for different groups and considered statistically significant when *p*-values were less than 0.05.

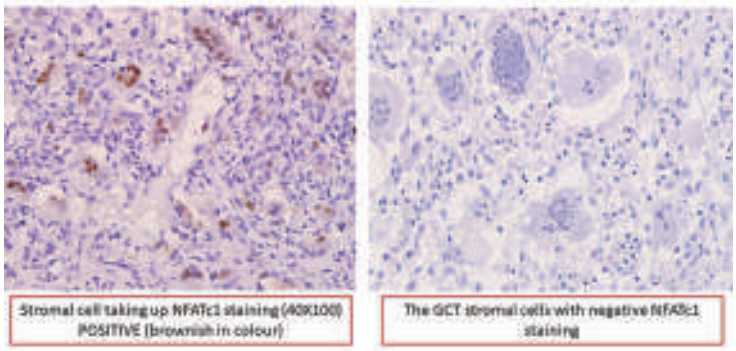
The mean value of NFATc1 expression obtained as a percentage of 1000 background cells was 0.81 with standard deviation of 1.48. The range was between 0.0 to 6.33 with a median of 0.07. Comparison of NFATc1 expression showed higher percentage in recurrence group with a mean of 1.01 (SD 0.68) compared to non-recurrence group with a mean of 0.79 (SD 1.55). The mean difference was 0.22 (-1.06, 1.51). This difference was statistically not. A comparison of NFATc1 expression showed higher mean value in lung metastases group which was 2.01 (SD 2.49) compared to 0.58 (SD 1.13) in non-lung metastases group. The mean difference between the two groups was 1.43 (-1.63, 4.49) which was also statistically not significant.

This study shows all 31 cases with aggressive stage III GCTB were not positively stained with NFATc1 antibody with the possibility osteoclast may have not been the main cells responsible in the bone destruction in GCTB condition.Further research may evaluate whether NFATc1may or may not be useful to predict the risk of pulmonary metastases or recurrence disease in Stage III GCTB.

Osteoclastic signalling pathway



NFATc1 expression



Group (n)	Mean (SD)	Mean difference (95% CI)	t-statistic* (df)	p
recurrence (3)	1.01 (0.68)	0.225	0.46 (4.6)	0.667
non-recurrence (28)	0.79 (1.55)	(-1.06,1.51)		

Group (n)	Mean (SD)	Mean difference (95% CI)	t-statistic* (df)	p
lung metastasis (5)	2.01 (2.49)	1.43	0.272 (4.32)	>0.00
non-lung met (26)	0.58 (1.13)	(-1.63, 4.49)		1

Effect of Brain Breaks Video on the Motives for the Physical Activity of Malaysians with Type 2 Diabetes Mellitus

Dr. Kueh Yee Cheng [yckueh@usm.my]
Department of Biostatistics and Research Methodology
School of Medical Sciences, Universiti Sains Malaysia

Brain Breaks video exercise is a promising intervention which has been developed by HopSports, an interactive youth physical education training system. These videos exercise known as Brain Breaks® Physical Activity Solutions or Brain Breaks for short. The Brain Breaks® engages and connects different social demographic level of community and individuals, schools and universities, the home, business, corporations, healthcare and government agencies. It delivers multiple streams of content simultaneously into fitness, education, entertainment, and interactive environments. These exercises are web-based structured physical activity (PA) breaks that are intended to stimulate an individual's health and learning. The exercises have been specifically designed for use in individual or group settings to motivate users to enhance their mental skills while providing the opportunity to be not only physically active but also to learn new motor skills, languages, works of art, music, and about different cultures. On the Global Community Health website, educators worldwide contribute by uploading exercise videos that suit their respective customs and cultures. These videos are then shared online and are accessible to anyone who would like to implement them. We developed several exercise videos based on Brain Breaks approach specifically for people with type 2 diabetes mellitus (T2DM). T2DM is the most common type of diabetes worldwide, with being physically inactive and overweight as main contributing factors. Motivation to PA is a crucial component to sustain T2DM patients to continue engage in exercise. We conducted a study to investigate the effect of using Brain Breaks video exercise to increase the motivation of T2DM patients in participating in PA, and hence increase their amount of PA.

The talk began by presenting several examples of Brain Breaks video exercise we applied on T2DM patients in Hospital Universiti Sains Malaysia (USM), Kubang Kerian, Kelantan. The participants for the study were T2DM patients who visited to their physician for their regular medical check-up appointment. Randomized controlled trial was performed in the study. The participants were randomized into experimental and control groups. At baseline, both the experimental and control groups were required to answer the Malay version of Physical Activity and Leisure Motivation Scale (PALMS-M) to evaluate their initial motives for PA. For the experimental group, participants were invited to join a WhatsApp group where the Brain Breaks videos were shared throughout the intervention phase. During the intervention, an exercise video of 10 minutes in length specifically designed for diabetes patients was uploaded to the WhatsApp group, and the participants were required to perform the exercise either outdoors or indoors (depending on their preference). They were reminded regularly as we uploaded a video every week. A different exercise video was given on the first day of each week in order to help participants avoid getting bored with the same exercise. Each of the experimental participants was given an adherence log-book for monitoring their progress. For the control group, the participants were given a brochure containing a brief introduction to the benefits of PA on health. The duration of the intervention was four months. At the end of each month, participants in both the experimental and control groups were required to answer the PALMS-M. The outcome of the study was based on the eight motives for PA as measured by the PALMS-M. Other than motives, we also measured the patients' amount of PA using the IPAQ-M. Similar to the PALMS-M, the patients were also required to answer the IPAQ-M five times (pre-, end of the first month, second month, and third month, and post-) during the intervention period.

The study involved a total of 70 T2DM patients. There were 37 participants in the experimental group, while the control group consisted of 33 participants. Patients' mean age was 57.8 (standard deviation = 8.5) and 55.7% were male.

In terms of motivation to PA, Table 1 shows the overall mean difference for all eight motives in the PALMS-M between the experimental and control groups. Overall, the experimental group had a higher mean for the motives than the control group. Based on the results, four out of the eight motives in the PALMS-M were significantly different between the two groups. Appearance, others' expectations, physical condition, and mastery were the motives that showed a significant difference between the groups. This indicated that Brain Breaks video exercise did have effect on improving the motivation to PA among T2DM patients.

Note. Table 1 is on the next page

Table 1. Overall mean difference of PALMS-M motives scores between experimental and control group.

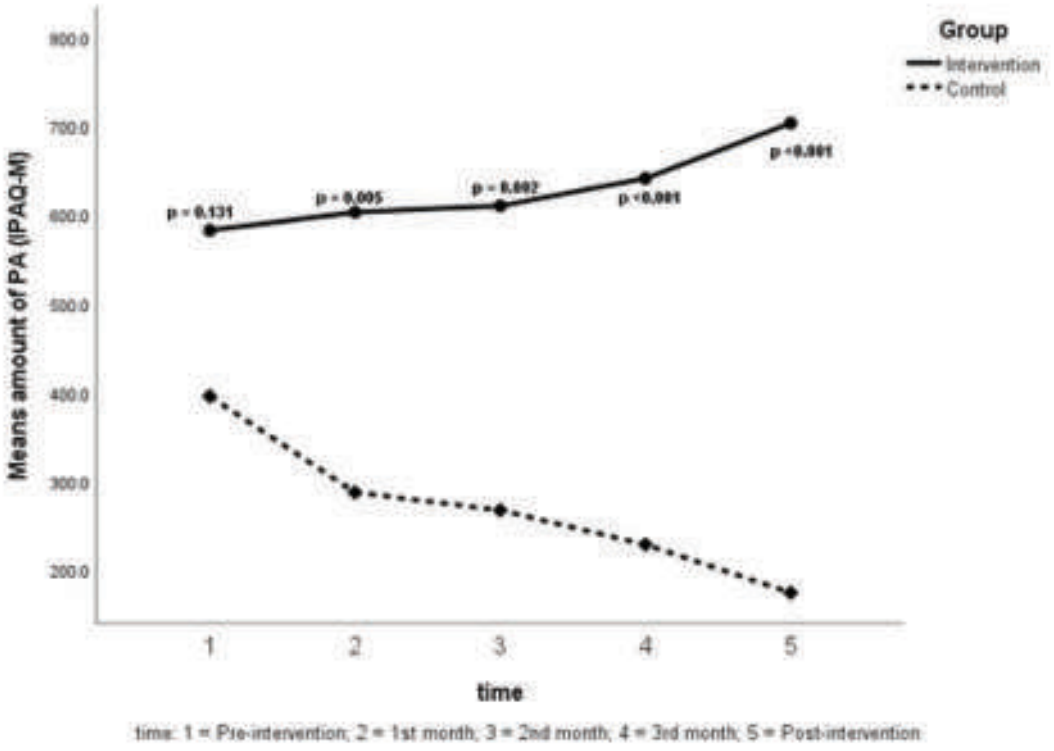
Comparison on PALMS-M motives (experimental and Control Groups)	Mean difference (95% CI)	*p*-value
Competition	1.17 (-0.19, 2.52)	0.090
Appearance	2.54* (0.53, 4.55)	0.014
Others' expectation	2.24* (1.27, 3.21)	<0.001
Affiliation	0.90 (-0.81, 2.62)	0.297
Physical condition	1.84* (0.26, 3.42)	0.023
Psychological condition	1.21 (-0.35, 2.78)	0.125
Mastery	2.16* (0.33, 3.98)	0.021
Enjoyment	0.93 (-0.80, 2.66)	0.288

Note. *Significant *p*-value, Repeated Measure MANOVA between two groups (with eight dependent variables: PALMS-M motives) was performed and no post-hoc comparisons between groups were done since there were only two group involved.

In terms of amount of PA, the experimental group produced a higher mean score in the amount of PA (measured by IPAQ-M) as compared to the control group, giving an overall difference with p-value of 0.001. Based on Figure 1, we can see that the difference between the two groups became more significant as time went along during the experimental period. The changes in the p-value in comparing the two groups, from pre- to post- experimental was from 0.131 to < 0.001.

We conclude that Brain Breaks videos can be considered as an effective intervention for motivating T2DM patients for PA. Appearance, others' expectations, physical condition, and mastery motives are all important for T2DM patients. The intervention with the Brain Breaks videos also helped to demonstrate differences in the trends for mean scores between the two groups, with the experimental group showing an upward trend and the control group showing a downward trend throughout the trial period. As for the PALMS-M, it is an effective scale for measuring the motives for PA of the participants. The Brain Breaks videos were also found to be effective for improving the patients' amount of PA, with both groups showing a significant difference after the intervention had finished. We suggested for future studies to involve more hospitals with improved sampling methods in order to include more participants. In addition, the consideration of more types of non-communicable diseases in the Brain Breaks exercise intervention trial would make the results more comprehensive and more generalizable to not only a single patient population but to other patient populations as well.

Figure 1. The PA amount changes of both group from Pre- to Post-intervention period



Note. Repeated Measure ANOVA between two groups (with one dependent variable: amount of PA) was performed

Tranexamic Acid for the Treatment of Gastrointestinal Bleeding: An International Randomised Double Blind Placebo Clinical Trial

Associate Prof. Dr Andee Dzulkarnaen bin Zakaria [andee@usm.my]
Department of Surgery, School of Medical Sciences
Universiti Sains Malaysia

Tranexamic acid reduces surgical bleeding and reduces death due to bleeding in patients with trauma. Meta-analyses of small trials show that tranexamic acid might decrease deaths from gastrointestinal bleeding. Halt-it trial research group; *Haemorrhage alleviation with tranexamic acid – intestinal system*, carried out a research to assess the effects of tranexamic acid in patients with gastrointestinal bleeding.

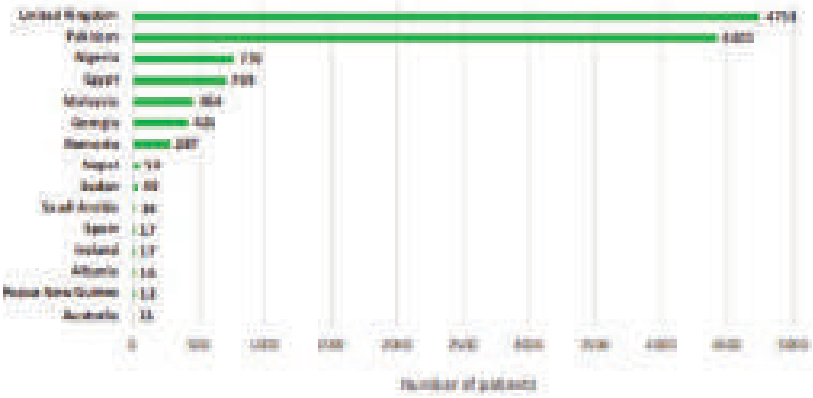
It was an international, multicentre, randomised, placebo-controlled trial in 164 hospitals in 15 countries. Patients were enrolled if the responsible clinician was uncertain whether to use tranexamic acid, were aged above the minimum age considered an adult in their country (either aged 16 years and older or aged 18 years and older), and had significant (defined as at risk of bleeding to death) upper or lower gastrointestinal bleeding. Patients were randomly assigned by selection of a numbered treatment pack from a box containing eight packs that were identical apart from the pack number. Patients received either a loading dose of 1 g tranexamic acid, which was added to 100 mL infusion bag of 0·9% sodium chloride and infused by slow intravenous injection over 10 min, followed by a maintenance dose of 3 g tranexamic acid added to 1 L of any isotonic intravenous solution and infused at 125 mg/h for 24 h, or placebo (sodium chloride 0·9%). Patients, caregivers, and those assessing outcomes were masked to allocation. The primary outcome was death due to bleeding within 5 days of randomisation; analysis excluded patients who received neither dose of the allocated treatment and those for whom outcome data on death were unavailable. This trial was registered with Current Controlled Trials, ISRCTN11225767, and ClinicalTrials.gov, NCT01658124.

Between July 4, 2013, and June 21, 2019, we randomly allocated 12 009 patients to receive tranexamic acid (5994, 49·9%) or matching placebo (6015, 50·1%), of whom 11 952 (99·5%) received the first dose of the allocated treatment. Death due to bleeding within 5 days of randomisation occurred in 222 (4%) of 5956 patients in the tranexamic acid group and in 226 (4%) of 5981 patients in the placebo group (risk ratio [RR] 0·99, 95% CI 0·82–1·18). Arterial thromboembolic events (myocardial infarction or stroke) were similar in the tranexamic acid group and placebo group (42 [0·7%] of 5952 vs 46 [0·8%] of 5977; 0·92; 0·60 to 1·39). Venous thromboembolic events (deep vein thrombosis or pulmonary embolism) were higher in tranexamic acid group than in the placebo group (48 [0·8%] of 5952 vs 26 [0·4%] of 5977; RR 1·85; 95% CI 1·15 to 2·98).

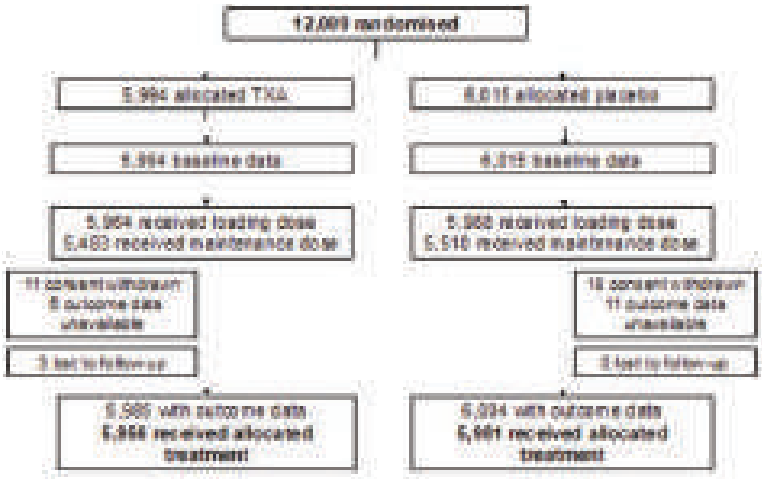
We found that tranexamic acid did not reduce death from gastrointestinal bleeding. On the basis of our results, tranexamic acid should not be used for the treatment of gastrointestinal bleeding outside the context of a randomised trial.

This research was funding by UK National Institute for Health Research Health Technology Assessment Programme.

Trial Recruitment by Country



Trial Profile



The Impact of Virtual Microscopy on Students' Knowledge Acquisition and Intrinsic Motivation

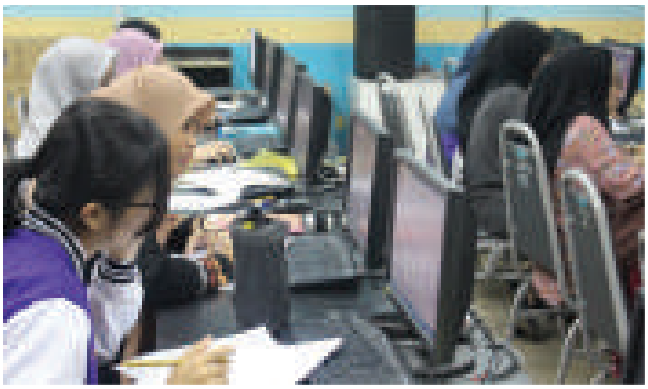
Dr. Fazlina Kasim [fazlinakb@usm.my]
Department of Anatomy
School of Medical Sciences, Universiti Sains Malaysia

A reduction in histology contact time after the medical education reformation had resulted in the integration or complete transition to virtual microscope in the histology curriculum. This study aims to compare the effects of using a virtual microscope and an optical microscope for learning histology among medical students in Universiti Sains Malaysia. One hundred and twenty medical students from 2017/2018 academic session were recruited. This was a one day intervention. All participants attended a lecture on 'Histology of the Eye' and then attended a slide demonstration session. Immediately after that, the students were divided into virtual and optical microscopy groups and were sent to their respective laboratories.

Knowledge acquisition was measured and compared between the study groups using the post-practical assessment score, changes in assessment scores and learning quotient score. Student perceptions of learning histology using respective learning tool were collected at the end of the day by administering the satisfaction survey and Intrinsic Motivation Inventory. Results revealed that both study groups, the virtual microscopy group (mean difference=38.508) and the optical microscopy group (mean difference=35.079) had significant changes in assessment score, $p < 0.001$. However, there was no significant difference between study groups in terms of level of comprehension (post-practical assessment) and learning ability (learning quotient score). The median (IQR) of satisfaction score for the virtual microscopy group [5.00 (1)] was significantly higher compared to optical microscopy group [4.00 (2)], p=0.008. For the intrinsic motivation inventory, only the perceived competence score of virtual microscopy group was significantly higher compared to the virtual microscopy group, p=0.037. There were no significant difference between the two study groups in terms of interest, pressure and value score.

In conclusion, the use of virtual microscopy as a learning tool gives students great satisfaction and perceived competence and also improved their knowledge in histology. Further investigation is needed to assess the comprehensive effect of virtual microscope in learning histology.

Practical Session: Virtual Microscope



Practical Session: Optical Microscope

Effectiveness of Balance Rehabilitation Using Bal Ex Quick Balance Among Persistent Postural-Perceptual Dizziness (PPPD) Cases

Dr. Zuraida Zainun [zuraidakb@usm.my]
Department of Neurosciences
School of Medical Sciences, Universiti Sains Malaysia

BAL EX Quick balance is an improvised and updated module body balance modified from BAL EX module Zainun Z (2019). This is a combination of Bal ex module with optokinetic stimulation, trampolin, exercise ball and BAL EXzz Foam. The main tool used in this module is the foam that able to support weight up to 120kg. The optokinetic stimulation using disco ball lamp was incorporated during this BAL EX Quick Balance therapy. Research shown that a rapid recovery of patients with chronic balance disorder can be treated when there is more challenges while doing the body balance training. A speed recovery using BAL EX QUICK BALANCE can be seen as compared to the original Bal Ex.

Persistence Postural perceptual dizziness (PPPD) is one of the common diagnosis among 30 to 50 years old age group. The main cause of this problem is a long-standing dizziness which is mainly vestibular problem. Psychological involvement is common among PPPD cases such as obsessive-compulsive, depression and anxiety. We reported a case of PPPD patient that underwent Bal Ex Quick Balance. Performing this case study able to emphasize and increase awareness among clinician regarding the PPPD especially dealing with middle age group that came with a typical vestibular symptom. Accurate diagnosis essentially important since it will greatly impaired the further management for every cases.

Figure 1. Bal Ex Innovation products

Figure 2. Intensive Bal Ex Quick balance intensive therapy

"My Secret Recipe" for Successful Research Projects

Prof. Dato' Dr Nik Hisamuddin bin Nik Ab Rahman [hisamuddin@usm.my]
Department of Emergency Medicine
School of Medical Sciences
Universiti Sains Malaysia

The presentation focused on my own experience over the last 18 years as a lecturer and clinical physician in achieving success in research projects in the field of Emergency Medicine throughout the career in the School of Medical Sciences, Health Campus, USM. The contents of the lecturer focused on few points:

i. Introduction to Methods and Ingredients of research work
ii. Interest in conducting research
iii. Collaborative research projects
iv. Supervisory work on research projects
v. Grants in research
vi. Miscellaneous factors

The introduction part consists of emphasis on general concept of any research work that was adopted by the presenter namely strict adherence to research cycle such as proper planning and execution of research project. (Figure 1) One of the crucial ingredients of research work is having interest in doing it. The presenter has given an example of his scholarly work of his particular interest over the last 20 years namely "road traffic injury" (RTI). As a result of this special interest, the presenter has successfully conducted few research projects pertaining to road safety and injury including scientific publication in international peer reviewed journals. One of his niche projects was on the application of Geographical Information System (GIS) and geo-mapping of RTI cases in Kota Bharu District. The project has created one PhD and three Master degree students and 5 peer reviewed journal publications.

The second crucial ingredient of research work is a robust collaborative work with internal or external agencies and organizations. The presenter has given two successful and excellent collaborative work examples. The Pan Asian Resuscitation Outcome Study (PAROS) and the Asia, Australia New Zealand Network Dyspnoea Study (AANZDEM) were of the two previous successful projects initiated by team in Singapore and Australia respectively in which the presenter was the Principle Investigator (PI) for both projects in Malaysia. In total the publication outcome for these two projects alone include 30 peer reviewed journal publications and sustained networking activities till present for any other research projects. The PAROS collaborative work involved 12 different countries across the Asian and Middle East countries. The PAROS group has also recruited a staggering sixty thousand patientssampling. AANZDEM on the other hand involved five countries in the region and patient sampling of five thousand cases. One of the most successful collaborative research network is the Clinical randomization of an anti-fibrinolytic in significant hemorrhage or known as the "CRASH 2 Trial" that involved over 60 nations world wide and over twenty thousand patient recruitment. This trial involved the use of Tranexemic Acid boluses in traumatic hemorrhage cases. The landmark trial has gained publication in the Lancet.

The third major ingredient for successful research work is student supervision. Student supervisory research work is an important source of good research outcome including paper publications. It is imperative that supervisors or lecturers must show good ethical and high standard supervision throughout the student candidacy.

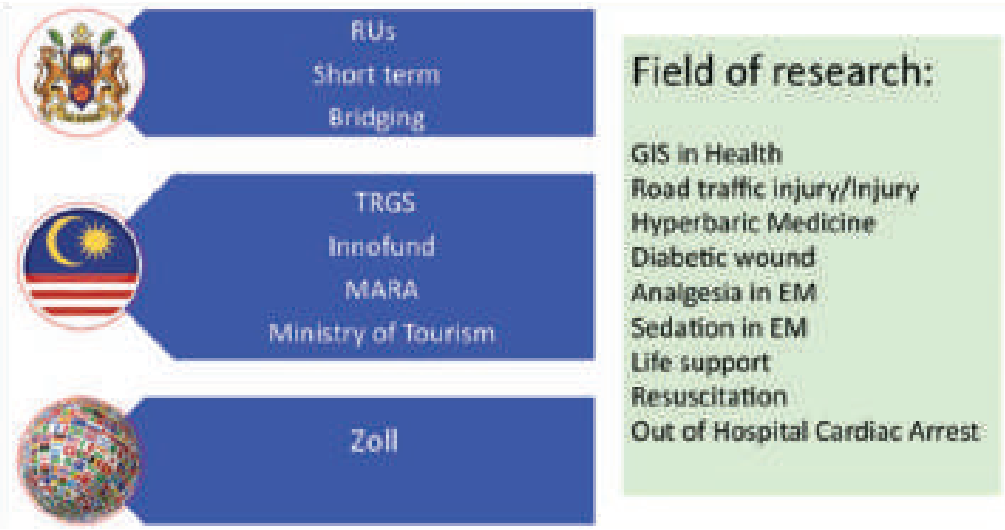
Figure 1: General research cycle

Avoidance of conflict of interest and manipulating students are of utmost importance. Throughout the career as a lecturer, the presenter has supervised over 50 students mainly in the clinical field of Emergency Medicine and has published over 20 papers as either a co-author or corresponding authors.

Other minor ingredients for successful research work include Grant procurement, team work and time management. Throughout his career, the presenter has obtained 20 research grants as both Principal Investigator and Co-Investigator. (Figure 2) Working in a team and optimum time management are crucial for a successful outcome.

As a conclusion, any research work requires a certain minimum amount of major ingredients and the minor components will add some "flavour" into it, creating hopefully a very successful output.

Figure 2: List of research grants secured by the presenter and his research fields



"One of the crucial ingredients of research work is having interest in doing it..."

Genetics, Historical & Cultural Perspectives in Defining the Malay Origin

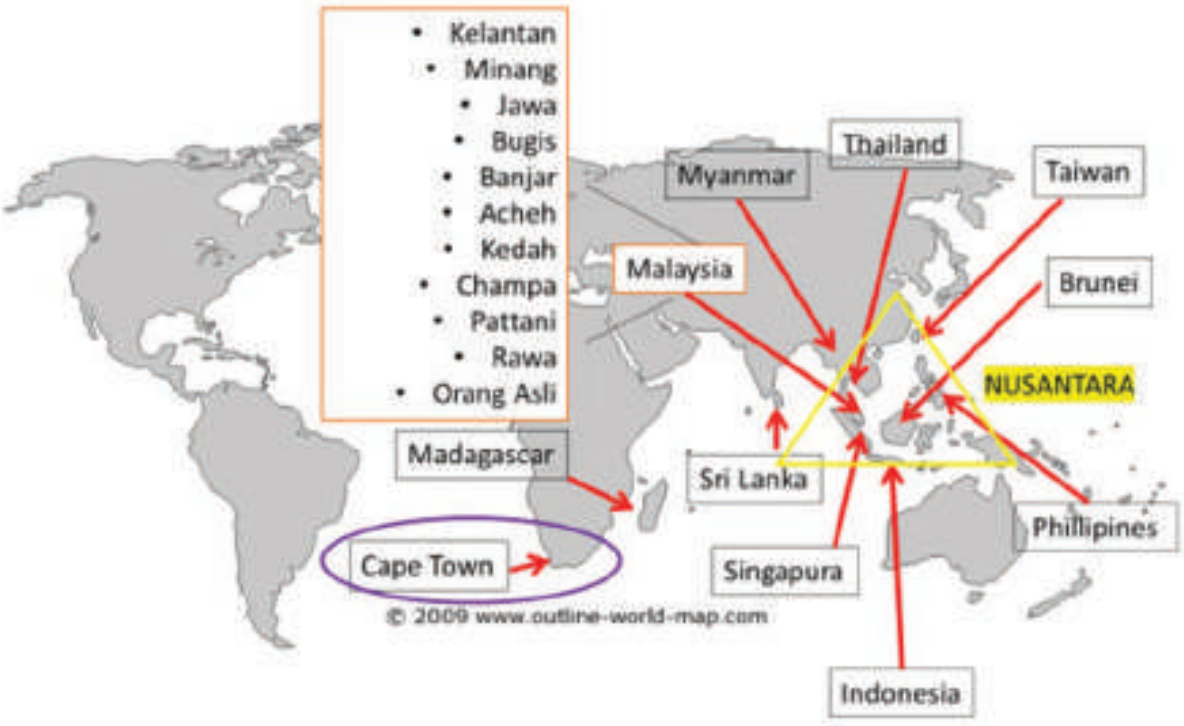
Prof. Dr. Zilfalil Bin Alwi [zilfalil@usm.my]
School of Medical Sciences
Universiti Sains Malaysia

According to the Constitution of Malaysia, Malays are Malaysian citizen, born and domiciled in Malaysia, professes the religion of Islam, habitually speaks the Malay language and conforms to Malay custom. Based on anthropology, Malays are an ethnic group of Austronesian people who speak Malayo-Polynesian language that belong to the Southern Mongoloid group of races and predominantly inhabit the Malay Peninsula (comprises of southern Thailand, Peninsular Malaysia, and the island of Singapore), south coast of Myanmar, eastern Sumatra, the coast of Borneo and the smaller islands between these locations – collectively known as the Alam Melayu. The aim of the study is to look at the ancestry and compare the genomic profile of the various subgroups of the Malay population and its relationship with linguistic factors.

Subjects were selected based on very strict criteria (at least three generations of the respective ethnic groups and no history of mix-marriage). Genetic analyses were carried out by DNA extraction from peripheral blood, various targeted polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP), DNA sequencing and genome-wide association studies (GWAS) by Affymetrix GeneChip® Microarrays technology. Ancestry-informative marker (AIM) Single Nucleotide Polymorphism (SNP) panel for Malay population was accomplished by bioinformatics analyses.

Based on the findings, Malays were found to be a heterogeneous population who shared genetic ancestry with Indonesian, Chinese Yunnan and some of the Proto-Malay (Orang Asli) groups in Peninsular Malaysia. Jawa Malay, Bugis Malay and Minang Malay have a very close genetic relationship with their Indonesian counterparts indicating a common ancestral history. Kelantan Malay formed a distinct group and showed close genetic relationship with the Indians and the Orang Asli Semang (Jahai and Kensiu) in Peninsular Malaysia. The northern Malays (Kedah Malay and Kelantan Malay) haplotypes could be found in either Indians or Chinese populations, indicating a highly admixture pattern among the populations. Nevertheless, the ancestry lines of the Malays, Indonesians and southern Thais were traced back to have shared a common ancestor with the Proto-Malays. Deutero-Malay also known as the Modern Malay is a descendant of Proto-Malay with admixture with Thai, Java, Sumatra, India and traders from China. In addition, whole genome sequence was carried out on two representatives from Kelantan Royal family in defining the Kelantan Malay which are much similar in ethnicity with the Pattani Malay from Thailand.

Figure 1: Malay population distribution in the world



Based on the study, Royal Kelantan Malays carry the SNPs which are associated with protection to Helicobacter pylori infection and beta-thalassemia. The Malay population study was expanded to linguistics, cultural and historical aspects outside Malaysia. A bigger study involving Makassar in Indonesia and Cape Malay in South Africa were achieved through an international grant. Cross-sectional study with in-depth interview was done across the Nusantara and Cape Town region. A moderate to strong genetic affinity based on the maternal gene pool of Nusantara and Cape Malays was shown as distribution of the mtDNA haplogroup display almost similar pattern. Both haplogroup M and H were identified in both populations. From linguistic and cultural affiliation aspect, Malays are a respected minority group and are said to be more trustworthy as the court would uphold Malays as reliable witnesses in legal cases. If food is taken as a cultural marker, the Cape Malay food culture has indeed fused with other minority groups as well as the locals. The strongest cultural linkage to the Malay heritage is religion. The Muslim identity is amalgated into the social construct of being a Cape Malay. The terms Malays and Muslims are used interchangeably. Furthermore, the Sufi Paradigm is one of the significant legacies of Sheikh Yusuf and Tuan Haji (both of whom originated from the Malay Archipelago), the two highly regarded early founders of Cape Malay spiritual-cultural heritage. Among the achievements from this Malay population study includes publications in indexed journals and presentation at conferences and seminars.

In conclusion, ongoing studies involving Malay populations from Cambodia, Thailand and Brunei continue to infer the strong correlation of genetic affiliations with highly statistical confidence with geographical demographic, cultural heritage, and history of Malay population in Nusantara region. Plans are in place to extend the study to Hawaii, Madagascar and New Zealand to look at the genetic link of the Malay population.

Acknowledgements

MyHVP Malay population study group

Special thanks to **Dr. Sharifah Nany Rahayu Karmilla Syed Hassan**, Post-Doctoral Fellow, Malaysian Node Human Variome Project (MyHVP), Universiti Sains Malaysia

Changing Research Landscape of Gut Health & Disorders: From Helicobacter pylori to Obesity

Professor Dr. Lee Yeong Yeh, MD, PhD.
Department of Medicine, School of Medical Sciences
Universiti Sains Malaysia

As a disease, obesity will be the greatest threat to humankind. The World Health Organization (WHO) estimates that at least 2.8 million people worldwide die from obesity each year. Worldwide prevalence of obesity nearly doubled from 1980 to 2008. 10% of men and 14% of women were affected in 2008 compared with 5% of men and 8% of women in 1980.

Malaysia has not escaped the epidemic. The national prevalence was 11.7% in those aged 15 years and above in 2004 compared to 4.4% in 1996. Malaysians are far more obese than any other South-East Asian citizen. Many of us would link obesity to heart disease, diabetes, and stroke, but many of us are unaware that obesity also affects the bowels.The landscape of gut diseases in Malaysia has shifted in parallel with the rising trend in obesity. One of them is gut cancers, and it is alarming to know that these cancers will increase by almost a third in the coming decade. A group of Asian experts, including myself, have found evidence that links obesity to various gut cancers, including large bowel cancer, cancer of the esophagus (the swallowing pipe), stomach cancer, liver cancer, and pancreatic cancer, and gallbladder cancer.

One of my most significant research work is to describe how obesity causes acid reflux disease, a disease that affects more than a third of the world population. Through my research, obesity appears to disrupt the function of the gastroesophageal junction, which is the lower part of the swallowing pipe before it enters the stomach. As a result, obese people have greater acid exposure, often silently, and later it increases their chances of developing esophagus cancer.

My current research work focuses on the gut microbiota, i.e., the balance of good and bad bacteria within our gut. One of our research has indicated that environmental factors, especially diet, are more important than genetics in determining the gut microbiota profile. Disturbance in composition and diversity of the gut bacteria can give rise to many gut diseases, e.g., Clostridium difficile colitis and beyond, including the brain and, of course, obesity.

Another of my recent research interest is functional gastrointestinal disorders or FGIDs. FGID is characterized by abdominal symptoms, including bloating but without the organic disease, and is often associated with meal or defecation. In collaboration with the Rome Foundation, our group has carried a nation-wide survey to determine the epidemiology of FGIDs among Malaysians. More than 2000 Malaysians and 73000 adults globally were surveyed. At least one FGID is found in 21.6%, and bowel disorders are the most common. Most importantly, the disease is associated with low quality of life and significant doctor visits.

Our researchers and doctors can do more. However, most importantly, we should start to think of gut health before cancer kills.

"Obese people have greater acid exposure, often silently, and later it increases their chances of developing esophagus cancer..."

Honey and Cancer: Understanding Its Anticancer Mechanism

Professor Dr. Nor Hayati Othman [hayatikb@usm.my]
Department of Pathology
School of Medical Sciences
Universiti Sains Malaysia

Honey could be considered the most sustainable food produced naturally. It contains sugars, vitamins, minerals and has high anti-oxidant activities. Cancer is on the rise in most countries. Carcinogenesis is a multi-step process and has multi-factorial causes. Among these are low immune status, chronic infection, chronic inflammation, chronic non-healing ulcers, smoking, obesity etc. Published studies thus far have shown that honey improves immune status, has anti-inflammatory and anti-microbial properties and promotes healing of chronic ulcers and wounds and scavenge toxic free radicals. We investigated the anti-cancer effect of Tualang (Malaysian jungle honey) and Manuka (Australian/New Zealand) honey and determined the mechanism of action.

The talk began by unfolding earlier research [in 2008] on honey where 2% and 10% of honey concentration were treated on confluent of oral squamous cells and human squamous cells cancer cell lines. That was the first study which illustrated the apoptotic effect of honey. Then data on early in-vivo study using 4 rats were shown in which rats that received carcinogen [DMBA] were treated with varying strength of honey [low medium and high doses]. This was the first in-vivo study clearly demonstrated the anti-cancer effect of honey. The talk later talked at great length on a more extensive on-vivo study. Sixty nulliparous female Sprague-Dawley rats were used for each phase of this 2-phase study.; the preventive study (phase 1) and the therapeutic study (phase 2); The animal groupings were as such: Group 0 (negative control); Group 1 (positive control); Groups 2, 3 and 4 received daily 0.2, 1.0 and 2.0 g/kg body weight of Tualang Honey (TH) respectively and group 5 received 1.0 g/kg Manuka Honey (MH). The rats of group 1,2,3,4 and 5 had cancer induction using carcinogen; 80mg/kg of methylnitrosurea (MNU). For the preventive phase, honey treatment was given one week prior to administration of carcinogen (MNU) and for the therapeutic study, honey treatment was given after breast cancers are palpable. The tumour growth is regularly monitored. Treatment was given for 120 days after which the rats were sacrificed and the tumour masses harvested. Histopathological examination and immunohistochemstry was done on these tumour masses against a panel of anti- and pro-apoptotic proteins. The hematological profile and serological examinations for all groups were performed. The results between honey treatment and non-treatment groups were analysed.

Both the preventive and the therapeutic phase show fairly similar result patterns. The rate of breast cancer progression is reduced in honey treated group compared to positive control group. The number of tumors developed was reduced and the tumor size were found to be smaller than those not given honey. The histological grading was also better. The mechanism by which TH and MH exert cancer-preventive and cancer-therapeutic effects is multifold; through improvement of immunological, hematological, serological response and by activation of the apoptotic pathway. There is up-regulation of pro-apoptotic proteins and down-regulation of anti-apoptotic proteins.

In conclusion, honey treatment before cancer induction gives better result than honey treatment after cancer development. Though honey may not have the capability to completely prevent development of breast cancers or to completely cure breast cancers, the scientific evidence shows that it retards tumour growth. The current anticancer agents are toxic to the body. Honey gives promising alternative strategy as an agent for prevention or as supplement to conventional therapy of breast cancer.

Figure 1: Compositions of honey

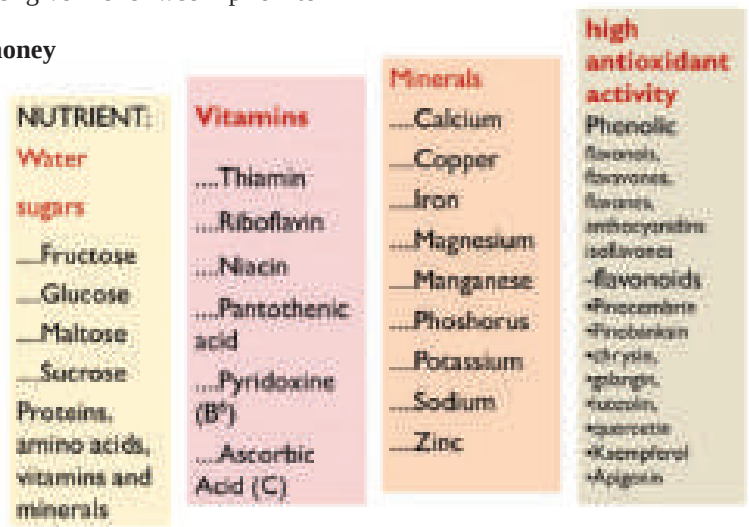
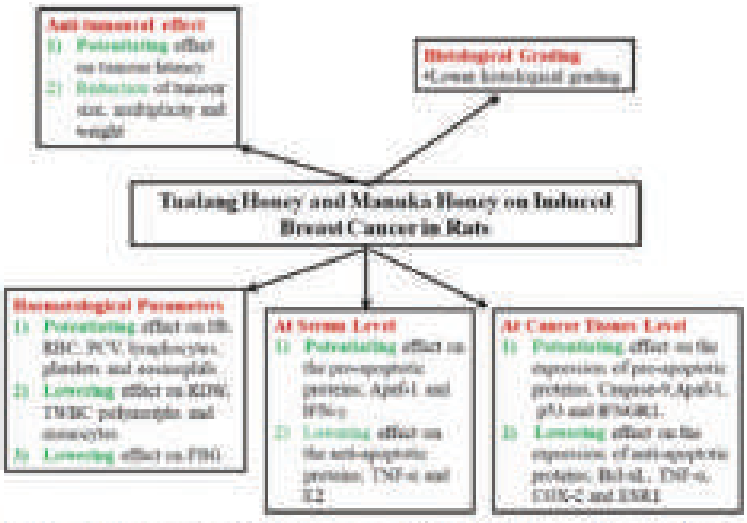
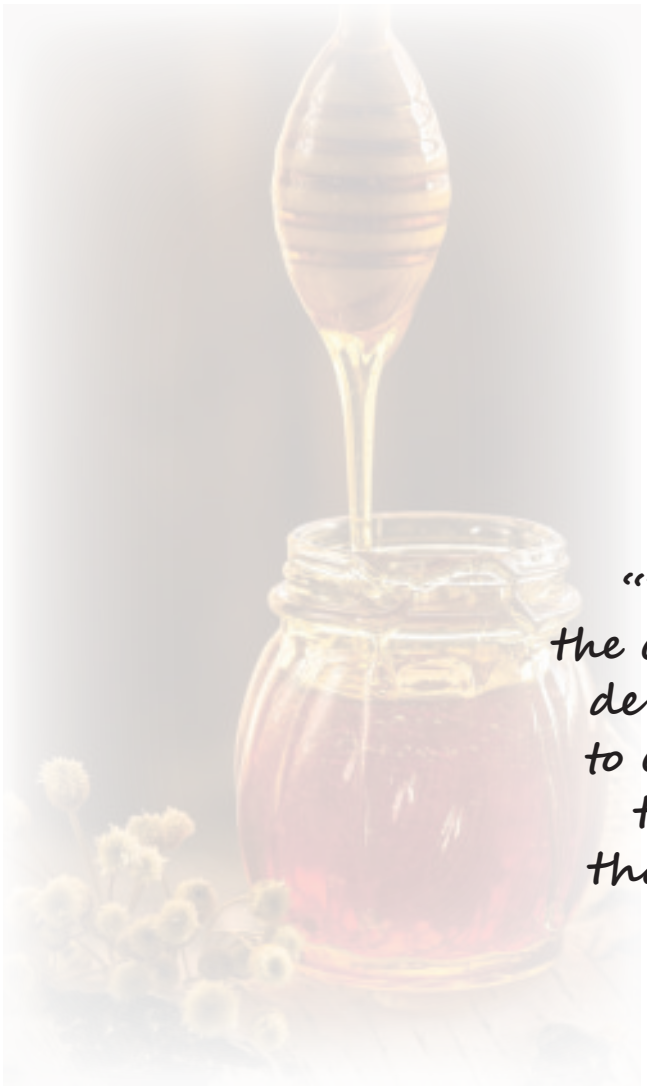


Figure 2: Schematic presentation of the summary of results (study I; honey treatment started BEFORE cancer induction





"Though honey may not have the capability to completely prevent development of breast cancers or to completely cure breast cancers, the scientific evidence shows that it retards tumour growth..."

Potential of TNF-TNFR2 Axis for Disease Therapeutics

Dr. Rohimah Mohamud [rohimahm@usm.my]
Department of Immunology
School of Medical Sciences
Universiti Sains Malaysia

My current research is focusing on the multidisciplinary fields consisting of immunoregulations in inflammatory diseases (cancer and allergy), infectious diseases (tuberculosis and COVID-19) and synthesis of different types of nanoparticles (polymersomes and Janus nanoparticles). This multidisciplinary field provides more opportunity for me to involve in multi-research studies and thus expand network with other researchers. Above all, my core project is investigating the role of tumour necrosis factor (TNF) targeting TNF-TNFR2 axis on regulatory T cells and dendritic cells in inflammatory and infectious diseases and modulation of nanoparticles on this axis (Figure 1).

I began the talk by highlighting the achievements that I have acquired for the past 6 years in PPSP. I had conducted a research on the effects of nanoparticles on mice dendritic cells which is covered by Short Term Research grant in 2015. I had successfully closed the grant on time and graduated one MSc student. This grant is important for me to establish nanoparticles research group in Immunology Department, which currently I have 6 students as main supervisor in my group (3 graduated, 2 ongoing PhD students and 1 ongoing MSc student). As for the translation from animal models to human patients, I had successfully secured a national grant (FRGS) in 2016 and successfully completed in 2020 without an extension on the duration.

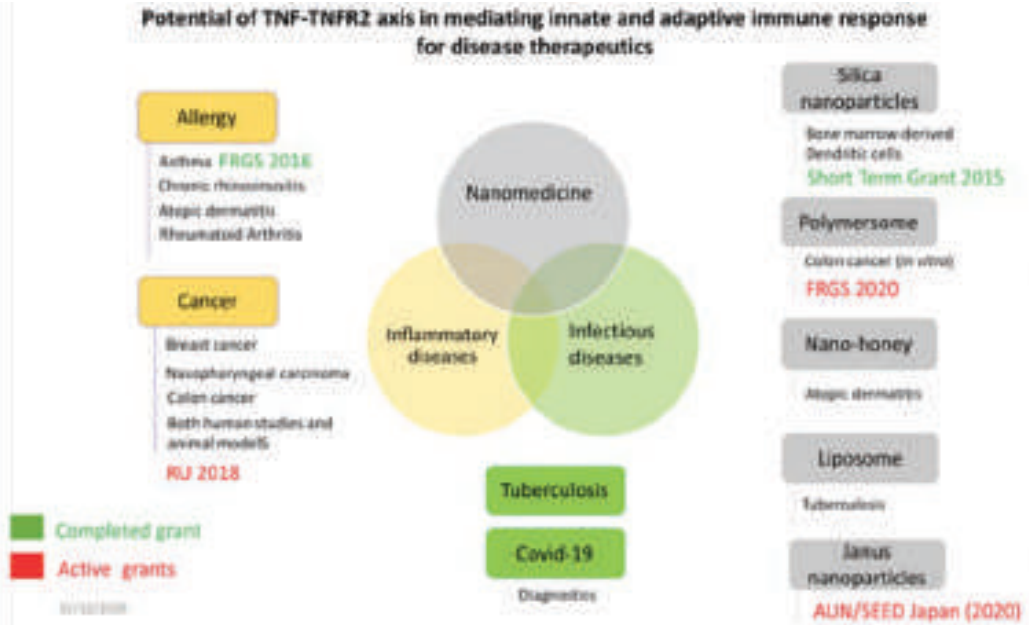
In 2018, I managed to secure a RU project for investigation of polymersomes in modulating the colon cancer by targeting TNFR2. This grant is conducted by 2 ongoing PhD students (Hatmal from Jordan and Hidayah) and will be completed early next year. Hatmal is the first international student in Immunology Department and Hidayah is the first student from Health Campus joining the co-tuttelle program in University of Lorraine. systemic toxicity and enhanced the specificity to target cell/tissue.

Later in the middle of the talk, I explained the importance on balancing our immune system and emphasized on the involvement of TNFR2$^+$ cells. I also mentioned the novelty of this research that is pioneered by Prof. Xin Chen from University of Macau, China. Besides, I have listed international researchers that have active collaborations with our group in Department of Immunology. Th whole research ideas are to establish a niche at PPSP focusing on the immunotherapeutics for all disease clusters. At the end of the talk, I proposed few studies on TNFR2$^+$ cells for FRGS 2021 grants.

A 10-year aim for RM's research group is:

Establish Immunotherapeutics Research Group for All Disease Clusters

Figure 1: The scope of RM's study at Department of Immunology



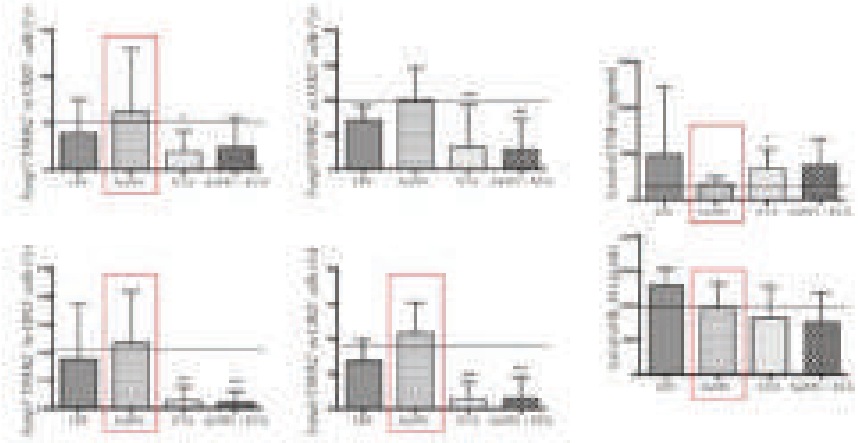
Nanoparticle in Asthma – via TNF-TNFR2 Axis

Dr. Suhana Ahmad [suhanaahmad1207@gmail.com]
Department of Immunology
School of Medical Sciences
Universiti Sains Malaysia

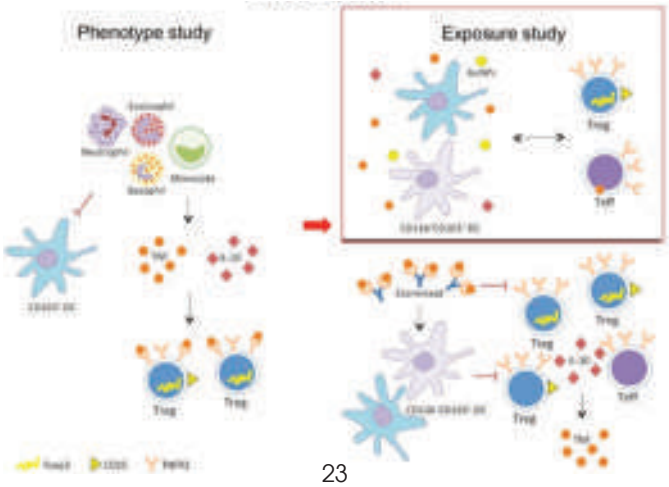
The talk began by introducing cell of interest in this study that is regulatory T cells (Tregs), which expressed TNFR2, one of the receptor of TNF. In our body, Tregs functioned by suppressing the excessive effects produced by other immune cells such as CD4 T cells, CD8 T cells and B cells, thus keeping balance in our immune system. Recently, a subset of Tregs that express TNFR2 has been shown to be more proliferative and suppressive than the negative population. Furthermore, TNFR2 is preferentially expressed on Tregs compared to other T cells and is crucial in the function and stability of Tregs.

In asthma, TNF play important role in the pathogenesis of asthma. They are secreted upon antigen challenge and continue to be responsible to the manifestations of asthma. One of the potential approaches in asthma therapy is to target Tregs including $TNFR2^+$ Tregs as it can inhibit several pathway of asthma pathogenesis. To target this $TNFR2^+$ Tregs, this study utilized nanoparticles (NPs) such as gold, as it is established that delivery of drug using NPs would minimize the systemic toxicity and enhanced the specificity to target cell/tissue.

Previously, the lymphocyte phenotype of this study asthma cohort has been described using flow cytometry platform. Compared to non-asthmatic cohort, current study asthma cohort is shown to exhibit inflammation through the increased of inflammatory mediators (TNF, eosinophils, basophils). However this asthma cohort also shown to have increased tolerance profile through Foxp3 in Tregs and IL-10 and it is suggested that the medication received by these patients have maintained the homeostasis and control the symptoms. As these medications just control the symptoms and do not modify the disease course, this study investigates the potential of immunotherapy in asthma using NPs as delivery tool. When we exposed PBMCs of asthma cohort, gold NPs remotely increased $TNFR2^+$ cells including $TNFR2^+$ Tregs and do not induce secretion of TNF. It is concluded that targeting TNFR2 with gold NPs does not induce toxicity towards our immune cells and they somehow provide the balance between Tregs and Teffs in this system, based the expression of TNFR2.



Overview



Thank You
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5. Assoc. Prof. Dr.
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6. Dr. Ruzilawati Abu Bakar

from

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MRP Team 2020

PROFESSOR DR. ROSLINE HASSAN
Advisor

MOHD ZAKI SELAMAT
Secretary

NIK FAUZI NIK ABDULLAH
Committee

MOHD DARIMI YUSOFF
Committee

KHAIRUL ZAHARI
Committee

ZULKEFLI SANIP
Committee

SOLAHASNI ABD AZIZ
Committee

TENGKU NOOR AYUNI HAZWANI TENGKU ALWI
Committee

DR. WAN FAIZIAH WAN ABDUL RAHMAN
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"Learn a lesson from the butterfly.
Don't be afraid of change but
change it beautifully..."

- MRP Team 2020 -

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