1st MALAYSIAN ASSOCIATION FOR CANCER RESEARCH
SCIENTIFIC CONFERENCE

"Cancer research in Malaysia: Is there a need for a paradigm shift?"

CONFERENCE PROGRAM BOOK

Main Organisers:
MACR | Malaysian Association for Cancer Research
MAHSA UNIVERSITY

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WELCOME MESSAGE FROM THE PRO-CHANCELLOR &
EXECUTIVE CHAIRMAN OF MAHSA UNIVERSITY

Distinguished guests, ladies and gentlemen, it gives me a great pleasure to warmly welcome all participants to the 1st Malaysian Association for Cancer Research (MACR) Scientific Conference 2019 (1st MSC). This conference is organised in collaboration with MACR, supported by Malaysian Universities, Research Institutes and Cancer Societies.

The 1st MSC with the theme: "Cancer Research in Malaysia: Is There a Need for a Paradigm Shift?" takes an in-depth look at the many issues raised by the cancer research community, highlighting quite importantly, the need for national cancer researchers and clinicians to work hand in hand foster collaboration, and examine the issues related to cancer research from in practice and also in research. This conference is a step towards achieving our vision in becoming a leading institution as centre of academic excellence in this region.

I am very certain that this conference will be able to provide a platform for strengthening our commitment towards new knowledge generation and interpersonal development. It is my aspiration that this conference will be a foundation for the growth of ideas towards a better tomorrow.

Last but not least, I would also like to congratulate all the organising committee members from MAHSA University, MACR, Universiti Putra Malaysia (UPM), UiTM, Monash University, Taylor’s University, Quest International University, Malaysian Oncological Society (MOS), National Cancer Society Malaysia, Forest Research Institute of Malaysia (FRIM) and Universiti Sains Malaysia (USM) iPPT for their tremendous teamwork effort in making the event a reality. With all the continued support and interest, I am sure that the quest of making MAHSA University a world class university is not impossible to achieve.

Thank you.

Professor Tan Sri Datuk Dr Hj. Mohamed Haniffa bin Hj. Abdullah
Pro-Chancellor & Executive Chairman
MAHSA University
WELCOME MESSAGE FROM VICE CHANCELLOR OF MAHSA UNIVERSITY

Assalamualaikum wbt and greetings, I would like to thank 1st Malaysian Association for Cancer Research (MACR) Scientific Conference 2019 (1st MSC) organisers for inviting me to address this conference. This 1st MSC conference, under the theme "Cancer Research in Malaysia: Is There a Need for a Paradigm Shift?", provides a platform to bring together to foster collaboration between cancer scientist, cancer research students and clinicians. With this platform, 1st MSC will embark on a whole process of making new discoveries and translating them into products and services in the oncology clinics.

I would like to congratulate the 1st MSC organisers for the achievement of attracting over 80 papers for this conference. Submissions received from 11 universities, 6 industrial companies and 9 different countries is a great achievement for MAHSA University and MACR. I am very happy to welcome all of you from United Kingdom, Australia, Hong Kong, Singapore, Sudan, Pakistan, India, Indonesia and Malaysia to this conference.

As one of Malaysia's Private Universities, MAHSA University’s main challenge is to remain competitive and relevant by offering high quality professional academic programmes and research activities, focusing on its niche areas. New knowledge and findings cannot be generated without any research and development activities. These efforts will undoubtedly generate lots of interesting results, new knowledge and hence bring further commercialisation activities.

On behalf of MAHSA University, I would like to express my appreciation to all Committee members of 1st MSC from the MACR and MAHSA University for their hard work and relentless effort. Without their commitment and contributions, this event would not been possible and successfully delivered at this time. I wish you all a fruitful discourse.

Professor Dato’ Dr. Ishak bin Abdul Razak
Vice-Chancellor
MAHSA University
WELCOME NOTE

It gives us great pleasure to welcome you to the 1st Malaysian Association for Cancer Research (MACR) Scientific Conference (1st MSC), which is held at MAHSA University, Bandar Saujana Putra, Selangor, Malaysia from 3rd – 4th December 2019.

‘Cancer Research in Malaysia: Is There a Need for a Paradigm Shift?’ is the theme of conference, highlighting quite importantly, the need for national cancer researchers and clinicians to foster collaboration, and examine the issues related to cancer research from all possible angles. Silos often exist unintentionally, but have been a real part of cancer research in Malaysia as there is no concerted effort to bring together various parties involved in cancer research in Malaysia. Hence, the needs for a paradigm shift to bridge the silos.

One such effort would be to foster collaboration between scientists and clinicians. Another would be to bring together many cancer researchers in the various parts of the country that are working in isolation and in small groups to form firm alliances. Our multidisciplinary programme covers a wide spectrum of areas in cancer research, including but not limited to: Cancer Biology, Translational Cancer Medicine, Clinical Oncology, Prevention & Control of Cancer, and Cancer Drug Discovery. We strongly believe that 1stMSC is the best platform to address these issues and provide solutions to take Malaysian cancer research to a higher level.

Besides improving our understanding of the biology of cancer to better detect and treat cancer, the team of expert speakers will also address some of the toughest challenges in cancer research from various perspectives. This is a platform for scientists and clinicians all over the world who are either working or interested in cancer-related fields to discuss common challenges and pragmatic solutions. The programme is structured to provide ample opportunity to interact with experts in the field and to network with fellow researchers to forge collaborative efforts, while the parallel sessions will equip you with valuable insights into building effective alliances across the various fields of research.

The Scientific Committee has planned a thorough programme with plenary-, invited-, parallel lectures and poster sessions. The highlight of the conference will be the awards for the Best Oral and Poster Presenters. We will also be hosting a Rising Star session on the 3rd December 2019 to highlight the outstanding careers of young cancer researchers.

Looking forward to meeting you at this conference!

PROFESSOR DR. JOHNSON STANSLAS
Advisor, 1st MSC
President, Malaysian Association for Cancer Research
Department of Medicine, Faculty of Medicine and Health Sciences, UPM

DR. AUDREY YONG
Co-Chair, 1st MSC
Deputy Dean (Research & Innovation)
Faculty of Pharmacy, MAHSA University

DR. MUTHUKKUMARAN A/L THIAGARAJAN
Co-Chair, 1st MSC
Oncologist
Hospital Kuala Lumpur
ORGANIZING COMMITTEE

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Dr. How Chee Wun
Dr. Alex Joseph Christopher
Ms. Pri Hansini Chaskar
PLENARY SPEAKERS

Prof. Sir David Lane
Chief Scientist
Agency for Science, Technology and Research (A*STAR), Singapore

Prof. Dr. Roger Phillips
Professor of Cancer Pharmacology
University of Huddersfield, UK

Prof. Dr. Anne Lee Wing-Mui
Clinical Oncologist
The University of Hong Kong, Hong Kong

Prof. Dr. Rosnah binti Mohd Zain
Professor of Oral Pathology & Oral Medicine
MAHSA University, Malaysia
INVITED SPEAKERS

Dato' Seri Dr. Mohamed Yusof Bin Hj Abdul Wahab
Surgeon and National Head
Clinical Services for General Surgery, Ministry of Health, Malaysia

Prof. Dr. How Soon Hin
Pulmonologist
International Islamic University, Malaysia

Prof. Dr. Hany Ariffin
Pediatric Oncologist
University of Malaya, Malaysia

Assoc. Prof. Dr. Chew Eng Hui
Medicinal Chemist
National University of Singapore, Singapore

Assoc. Prof. Dr. Fazlul Huq
Medicinal Chemist
University of Sydney, Australia

Assoc. Prof. Dr. Ho Gwo Fuang
Clinical Oncologist
University of Malaya, Malaysia

Assoc. Prof. Dr. Nirmala Bhoo Pathy
Cancer Epidemiologist
University of Malaya, Malaysia

Assoc. Prof. Dr. Yap Lee Fah
Molecular Biologist
University of Malaya, Malaysia

Dr. Alan Khoo Soo Beng
Cancer Researcher
Institute of Medical Research, Malaysia

Dr. Sucharit Pongprakyun
Clinical Oncologist
Hospital Wanita Dan Kanak-Kanak Sabah, Malaysia

Dr. Muralitharan Munisamy
Director
National Cancer Society Malaysia, Malaysia

Dr. Ong Tee Chuan
Clinical Haematologist
Hospital Ampang, Malaysia

Dr. Marfu’ah Nik Eezamuddeen
Clinical Oncologist
Universiti Teknologi Mara, Malaysia
### Theme: “Cancer Research in Malaysia: Is There a Need for a Paradigm Shift?”

#### Conference Day 1 (3rd Dec 2019)

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Constrained Peptides and Mini Proteins as Novel Therapeutics Targeting p53  
**Professor Sir David Lane**  
Venue: The Ballroom |
| 945   | **Invited Talk 1**  
Epstein-Barr Virus and Nasopharyngeal Carcinoma  
**Associate Prof. Dr. Yap Lee Fah**  
Venue: The Ballroom |
| 1010  | **Invited Talk 2**  
Pre-clinical models for the study of nasopharyngeal carcinoma  
**Dr. Alan Khoo Soo Beng**  
Venue: The Ballroom |
| 1035  | Morning Tea Break & Networking |
| 1055  | Poster Viewing & Judging Session 1  
Networking  
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| 1125  | **Parallel Sessions**  
Each Oral Presentation - 10 min/ Q&A - 5 min |
| 1250  | **Lunch Talk by Novartis**  
Reimagine Medicine – Collaborating to Deliver Innovation  
**Dr. Balraj Sethi**  
Venue: The Ballroom |
| 1350  | **Plenary Session 2 (Clinical Oncology)**  
My Journey in Research on Nasopharyngeal Cancer  
**Professor Anne Lee Wing-Mui**  
Venue: The Ballroom |
| 1435  | **Sponsored Talk 1 (Agilent)**  
Tools and Workflows for Clinical and Translational Research in Cancer  
**Robin Philp** (Academia & Collaborations Manager, SEA)  
Venue: The Ballroom |
| 1455  | **Invited Talk 4**  
Immunotherapy for Solid Cancers: An Update  
**Associate Professor Dr. Ho Gwo Fuang**  
Venue: The Ballroom |
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Metastatic Gastric Cancer - Molecular & Clinical Updates  
**Dr. Sucharit Pongprakyun**  
Venue: The Ballroom |
| 1545  | Afternoon Tea & Networking |
| 1605  | **Invited Talk 6**  
From Trials to Bedsides and vice versa – the Real-Life Hurdles in Hematologic Malignancies  
**Dr. Ong Tee Chuan**  
Venue: The Ballroom |
| 1630  | **Invited Talk 7**  
Impact of Research in Supportive Care in Oncology  
**Dr. Marfu’ah Nik Eezamuddeen**  
Venue: The Ballroom |
| 1655  | **Rising Stars**  
Venue: The Ballroom |
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**Conference Day 2 (4th Dec 2019)**

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<td><strong>Invited Talk 11</strong>&lt;br&gt;Can combination with phytochemicals make platinum drugs more desired and welcome?&lt;br&gt;<em>Associate Professor Dr. Fazlul Huq</em>&lt;br&gt;Venue: The Ballroom</td>
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*Disclaimer: All are subject to change*
PLENARY SPEAKER (CANCER BIOLOGY)
Date: 3rd December 2019
Time: 9.00 am - 9.45 am
Venue: The Ballroom

Constrained Peptides and Mini Proteins as Novel Therapeutics Targeting p53

Prof. Sir David Lane FRS

Many important targets for human therapy are deemed “difficult” because of their intracellular location and lack of binding sites for small molecules. This problem is now being addressed by developing new larger molecules that can for example act as excellent inhibitors of protein-protein interactions or promote the correct folding of mutant proteins by acting as molecular chaperons. The p53 pathway provides an outstanding target and test system for these new approaches and we have used synthetic biology methods to develop powerful reporter systems. The challenge of these larger molecules that includes stapled and cyclic peptides, monobodies and other mini-protein domains is ensuring their effective entry into the correct intracellular compartment. The study of natural products and toxins is providing novel insights into this process and the ability of synthetic biology and protein evolution methods to access huge libraries of variants of mini proteins and constrained peptides suggest that a whole new synthetic pharmacy is within reach. Most progress has been made using hydrocarbon stapled peptides where the first generation of molecules that bind and inhibit Mdm2 and Mdm4 and thus activate p53 as a transcription factor are in clinical trial. In this model second generation molecules of great specificity and potency are being developed using novel stapling methods, unnatural amino acids and new delivery methods.

INVITED SPEAKER (CANCER BIOLOGY)
Date: 3rd December 2019
Time: 9.45 am - 10.10 am
Venue: The Ballroom

Epstein-Barr Virus and Nasopharyngeal Carcinoma

Associate Prof. Dr. Yap Lee Fah

It is over 50 years since the Epstein-Barr virus (EBV), the first human cancer virus, was discovered. EBV is the most common persistent virus infection in humans with around 95% of the world’s population sustaining an asymptomatic lifelong infection. The closest association with EBV infection is seen in undifferentiated nasopharyngeal carcinoma (NPC), a cancer type that is particularly prevalent in southern China and Southeast Asia, including Malaysia. Indeed, many unique characteristics of NPC could be attributable to the virus. The presence of EBV in every tumour cell provides opportunities for biomarker and therapeutic intervention including immunotherapy and/or targeting pathways activated by EBV latent proteins. Recent studies have profiled the mutational landscape of NPC and identified more heterogeneity in the pattern of EBV gene expression than previously suggested. This talk will highlight the contribution of EBV to the pathogenesis of NPC and discuss the exciting prospects for the development of novel treatment strategies for NPC patients.
INVITED SPEAKER (CANCER BIOLOGY)
Date: 3rd December 2019
Time: 10.10 am - 10.35 am
Venue: The Ballroom

Pre-clinical Models for the Study of Nasopharyngeal Carcinoma

Dr. Alan Khoo Soo Beng

Cancer Research Centre, Institute for Medical Research, National Institutes of Health, Ministry of Health Malaysia, 1 Jalan Setia Murni U13/52, Setia Alam, 40170 Shah Alam, Selangor, Malaysia

Cell and animal based studies form an important component of cancer research. In vitro and in vivo models are used to study the gene function as well as to study potential targets for therapies. Evidence of drug efficacy in pre-clinical models are useful to justify clinical trials to test candidate drugs.

Nasopharyngeal carcinoma (NPC) is a major cancer in Malaysia. Translational research in NPC is hindered by the limited number of cell lines for in vitro and in vivo studies. Our group have been developing patient-derived xenografts from NPC patients. These PDXs were extensively characterised by histology, immunohistochemistry, EBER in situ hybridization, DNA finger printing, whole genome sequencing, RNASeq as well as RNAScope. The xenograft cells were also grown in short term in vitro 2D and 3D culture systems. The xenograft cells were labelled with GFP-luc2 for in vitro co-culture assays as well as to model skull base invasion (T4 disease) and distal metastasis (M1 disease) in mice. These cells would serve as useful resources for translational research in NPC.

PLENARY SPEAKER (CLINICAL ONCOLOGY)
Date: 3rd December 2019
Time: 1.50 pm - 2.35pm
Venue: The Ballroom

My Journey in Research on Nasopharyngeal Cancer

Prof. Dr. Anne Wing-Mui Lee

My journey started under the inspiration of my first mentor Prof. John Ho, one of the greatest pioneers on nasopharyngeal cancer (NPC). He taught us that cancer treatment must be evidence-based; and if data is lacking, we should initiate our own research. For NPC, with its uniquely skewed distribution, Asian centers play a key role in the needed research. I started my research to address questions most frequently encountered in clinical management. As a medical doctor working in a busy government service departments, without research grants and supports by other university scientists, the challenges and limitations are obviously formidable. With perseverance and concerted team efforts, we managed to come up with useful messages covering the whole spectrum of clinical issues from staging & prognostication, radiotherapy techniques and dose fractionation, chemotherapy sequence and regimen, late toxicities, and management of recurrence.

In more recent years, I also attempt to conduct studies that can have impact on global health policy and international standards. Furthermore, with taking up of academic post, I began to participate more in translational studies in collaboration with scientists and virologists.

This talk is aimed at sharing of my experience, particularly with young researchers. Summary of my research on NPC and the lessons that I have learnt along my journey will be presented.
Immunotherapy for Solid Cancers: An Update

Assoc. Prof. Dr. Ho Gwo Fuang

Harnessing the body’s ability to mount an immune response against cancer cells is now a well-established strategy to treat cancers. It has been known for many years that the immune system can help to treat cancer; however, initial attempts to utilize its potential had not gain widespread use.

Recently, interest in this strategy has increased, as a result of two main areas of breakthrough:

1. Checkpoint inhibitors using antibody against programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1)
2. Chimeric antigen receptor (CAR) T-cell therapy

Remarkable success has been achieved with many tumour types: pembrolizumab, an anti-PD1 antibody, is approved for treatment of melanoma, non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), head and neck squamous cell carcinoma, classical Hodgkin lymphoma, primary mediastinal large B-cell lymphoma, urothelial carcinoma, microsatellite instability-high (MSI-H) cancer, gastric cancer, oesophageal cancer, cervical cancer, hepatocellular carcinoma, Merkel cell carcinoma, renal cell carcinoma, and endometrial carcinoma.

An anti-PD-L1 antibody, atezolizumab, is indicated for the treatment of advanced urothelial carcinoma, NSCLC, SCLC, and for use in combination with abraxane for the treatment of metastatic triple-negative breast cancer.

Despite its impressive result in some patients, checkpoint inhibitors do not work for most patients, with single agent response rate ranging between 10–40%. The search is on for better predictor of response apart from the known PDL-1 and MSI-H, as well as to improve response rate using combined approaches. Tumour mutational burden (TMB) load, gut microbiome, tumour-infiltrating CD8+ lymphocytes and specific gene signatures are some of the candidate biomarkers.

Combining anti-CTLA-4 and anti–PD-1 therapies has been shown to be associated with meaningful survival improvements, and inhibition of CTLA-4 activates T-cell immune responses, leading to a potentially synergistic effect with PD-1/PD-L1 inhibitors. This strategy has been shown to be effective in treating melanoma and NSCLC.

Combining immunotherapy and chemotherapy is now a proven strategy for NSCLC and breast cancer.

Combining immunotherapy and targeted therapy is effective for renal cell carcinoma (axitinib and pembrolizumab), endometrial and hepatocellular carcinoma (lenvatinib and pembrolizumab). This approach is currently investigated for multiple tumour sites.

Despite achieving great success in leukaemia, CAR-T cell therapy has so far made limited impact in solid tumours, with the main limiting factor being tumour heterogeneity. Other T cell approaches: tumour-infiltrating lymphocytes and adoptive T cell transfer, have reported success in small studies in ovarian cancers and nasopharyngeal and head and neck cancers.

Approaches using cancer vaccine: single tumour antigen (peptide, nucleic acid or protein) or multiple antigens (pulsed dendritic cells, whole tumour cell) are still under investigation, with many failed attempts encountered despite initial phase 2 successes. Approaches that utilise tailor-made vaccine, using patient’s own tumour are more likely to be successful, but are much more labour intensive.
Next generation immunotherapy is now subject of intense research, with immune agonist and Bi-specific T-cell (BiTEs) the two main approaches. BiTEs form a link between T cells and tumour cells, causing T cells to exert cytotoxic activity on tumour cells, independent of MHC I or co-stimulatory molecules.

**INVITED SPEAKER (CLINICAL ONCOLOGY)**
Date: 3rd December 2019  
Time: 3.20 pm - 3.45 pm  
Venue: The Ballroom

**Metastatic Gastric Cancer - Molecular & Clinical Updates**
Dr. Sucharit Pongprakyun

Metastatic gastric cancer remains one of the more challenging cancers to treat. According to the GLOBOCAN 2018 data, it is the third most common cause of cancer death worldwide. In Malaysia, it is the 8th most common cancer among males and 10th most common cancer among females but ranks as the 6th most common cause of cancer death for 2018. It has been reported that majority of cases in Malaysia are detected at an advanced stage. Early detection followed by the appropriate treatment would help to improve the survival of patients. Chemotherapy has been used as the mainstay of treatment for many decades in advanced/metastatic disease. The emergence of newer class of drugs such as monoclonal antibodies and immunotherapy have broaden the scope of treatment options available. However, the survival rates although improved with the presence of newer agents, have remained dismal. Specific biomarkers discovered such as HER2 has allowed a more targeted-based treatment to be used in subtypes which harbor this biomarker. It is important to explore further the role of biomarkers in gastric cancer and to be aware of biomarkers currently been used in clinical practice, in clinical trials and in various stages of research.

**INVITED SPEAKER (CLINICAL ONCOLOGY)**
Date: 3rd December 2019  
Time: 4.05 pm - 4.30 pm  
Venue: The Ballroom

**From Trials to Bedsides and vice versa - the Real-Life Hurdles in Hematologic Malignancies**
Dr. Ong Tee Chuan

Evidence based medicine has shaped the current practice of modern medicine, and it has transformed the image of “bloodletting-all” doctor to a modern physician who practices with scientific basis and backed up by clinical trial data. Perhaps a physician-scientist is the best bridge to the gap of basic science knowledge and clinical medical practice, as he can play a 2-in-1 role seamlessly. Academic medicine in the teaching university hospital has traditionally been the cradle for producing physician-scientist, but we do see the push for this culture into public and private service hospitals in recent years. However, the culture of "publish or perish" and "p value obsession" are now being identified as possible unintended consequences of emphasizing evidence based medical practice. Some of these issues will be discussed in this short talk.
Impact of Research in Supportive Care in Oncology

Dr. Marfu'ah Nik Eezamuddeen

Over years, we have seen therapeutic advances enabling better survival in cancer patients. This progress has placed an emphasis on the dimension of supportive care in cancer. Supportive care in cancer is the prevention and management of adverse effects of cancer and its treatment. This entity looks into the symptom management of physical, psychological and treatment toxicities across the continuum of the cancer experience: from diagnosis, through treatment, to post-treatment care.

Prevention or reduction of treatment side-effects translates into improvement in therapy tolerance and compliance, thus increasing benefits of active therapy. Nausea and vomiting, a major symptom affecting cancer patients, can be induced by chemotherapy or radiotherapy, or can be part of advanced cancer. The latest guidelines in antiemetic use have included the role of new NK1 receptor antagonists, rolapitant and netupitant, the latter given in combination with palonosetron (NEPA), and the use of olanzapine.

Oral complications secondary to cancer therapy, including mucositis which may affect any part of the digestive tract depending on type of cancer therapy significantly causes distress to patients and caregivers. Extensive research has been made looking into successful interventions for mucositis – anti-inflammatory agents, vitamins, photobiomodulation techniques to name a few – in hope to enable patients to tolerate complications of treatment without compromising quality of life.

Cancer-related fatigue significantly disrupts normal functioning and quality of life for a substantial portion of cancer patients, and may persist for years following cancer therapy. It is the most widespread adverse effect of cancer in adults and children. Meta-analysis of randomized controlled trials of pharmaceutical therapies for cancer-related fatigue reveal a small effect size for all drug classes. Exercise interventions has been more promising. Exercise was found to significantly improve both quality of life and physical function in cancer patients.

There are many other aspect of supportive care in cancer that are growing in interests. Sexual health issues, survivorship and digital healthcare are among contemporary subjects with promising research potential. Alleviation of symptoms and complications of cancer and its therapy makes excellent comprehensive cancer care possible.

The Preclinical and Clinical Development of Apaziquone (EO9) as a Locoregional Therapy for Non-muscle Invasive Bladder Cancer

Professor Dr. Roger Phillips

The development of anti-cancer drugs is a difficult and challenging enterprise that induces excitement and disappointment in equal measure. This is particularly true in the case of
Apaziquone (originally known as EO9) which was originally synthesised by Oostveen and Speckamp in the 1980’s at the University of Amsterdam. Following promising preclinical studies, EO9 underwent clinical evaluation in the 1990’s but no complete or partial responses were observed in phase II studies following intravenous administration. The reason for its failure was attributed to poor drug delivery to tumours caused by (i) rapid pharmacokinetic elimination and (ii) poor penetration through avascular tissue. Whilst these properties are clearly unsuitable systemically administered drugs, they are paradoxically ideal for loco-regional therapies where the aim is to have high levels of drug at the site of drug administration. Based on this understanding, a further clinical trial of EO9 against non-muscle invasive bladder cancer (NMIBC) was developed on the basis of (i) intravesical administration of EO9 into the bladder would circumvent the drug delivery problem (ii) retention within the bladder for one hour would increase the duration of drug exposure and (iii) any drug reaching the circulation would be rapidly eliminated thereby reducing the risk of systemic toxicity. Significant anticancer activity was reported in phase I and II clinical trials (67% complete response rate) and this presentation will conclude by describing the current clinical status of EO9 against NMIBC and discussing the implications of this work for drug discovery and locoregional therapies.

INVITED SPEAKER (CANCER DRUG DISCOVERY/ TRANSLATIONAL)
Date: 4th December 2019
Time: 9.15 am - 9.40 am
Venue: The Ballroom

Translating research into personalized therapy for childhood acute lymphoblastic leukaemia

Prof. Dr. Hany Ariffin

Acute lymphoblastic leukaemia (ALL) is the commonest paediatric malignancy, representing a third of all cancers in children. From being a uniformly fatal condition in the 1950s, childhood ALL has become one of the greatest success stories of cancer treatment history. Overall survival rates of >90% have been realized largely through the systematic conduct of multi-institutional clinical trials, improved knowledge of disease biology, along with increased expertise in supportive care. However, the journey to reach these outstanding achievements began with the breakthrough discovery of the folate antagonist, aminopterin, where it was used as monotherapy. Subsequently, more drugs were discovered leading to the development of combination therapies using cytotoxic agents of various classes. In tandem with drug discovery, research into discovering the heterogeneity of leukemic blasts and exploiting these for therapeutic gain was actively pursued. Subsequently, preservation of normal growth and development in affected children became an equally important benchmark for success. Thus, sequentially developed treatment protocols for ALL, as with for most other paediatric cancers, shifted focus to achieving a better balance between improving cure and reducing toxicities. Therapy was risk-adapted and increasingly personalized to reduce late-effects – the latter is now a major area of research due to the large population of survivors of this previously fatal disease. Modern oncology therapy dictates that there is no longer a ‘one-size-fits-all’ way of managing patients with various cancers and childhood ALL is one of the earliest cancers where disease biology determined, and continues to drive, treatment choices.
Making advanced Non-Small Cell Lung Cancer (NSCLC) into chronic disease: What scientists can do?

Prof. Dr. How Soon Hin

Lung cancer is one of the most common cancer, it accounts for about 10% of all cancer cases but associated with 20% of cancer mortality. Most lung cancer patients presented at the late stages. In Malaysia, 90% of them were diagnosed with either stage III or IV at presentation. In the era of chemotherapy, overall survival of treated advanced NSCLC was 9-12 months. The discovery of driver mutation eg. EGFR, ALK, ROS 1 significantly prolong its survival. In profile 1014 study, median overall survival of ALK positive NSCLC patient treated with ALK inhibitors was extended to more than 4 years. In the same study, patients treated with chemotherapy without ALK inhibitor were associated with poorer outcome. In the recent years, immunotherapy had been showed to prolong overall survival of patients with NSCLC without driver mutation. Some of patients who were given immunotherapy had durable response and possible cure. With discovery of more therapeutic agents, better molecular diagnostic tools and improvement in efficacy of current treatment, advanced NSCLC may become chronic disease in future. Scientists play an important role to achieve this goal.

The Thiorredoxin System – A Friend or Foe in Disease States and Its Relevance as a Target in Anticancer Treatment

Assoc. Prof. Dr. Chew Eng Hui

The thioredoxin and glutathione systems are the two major thiol redox systems that maintains intracellular redox homeostasis. The thioredoxin (Trx) system comprises Trx, thioredoxin reductase (TrxR) and NADPH. TrxR catalyzes the NADPH-dependent reduction of the active site disulfide of oxidized Trx. To protect cellular proteins from oxidative damage, Trxs use a conserved redox active dithiol/disulfide motif (-Cys-xx-Cys-) to participate in reversible thiol-disulfide exchange reactions. Emerging findings have indicated that the dysregulated levels of the components of the Trx system has led to different disease states. Our laboratory has taken the interest to investigate the Trx system’s involvement in regulating apoptosis and it has been found that thioredoxin-1 (Trx-1) is capable of regulating DNA damage mediated by apoptosis inducing factor (AIF). The identification of the interaction between Trx-1 and AIF has provided opportunities to design and develop strategies that either promote or prevent this protein-protein interaction for treatment of different disease states. While Trx is required for regulation of cell proliferation and apoptosis, on the other hand, in cancer, the biological effects of the Trx system contribute to tumor growth and progression. In the light of the high prevalence of cancer and refractoriness of malignant tumors to clinical agents, novel molecular targets need to be identified.
and new chemotherapeutics be discovered. Accumulating evidence has indicated that the selenocysteine-dependent TrxR enzyme is a valid molecular target for anticancer drug development. Numerous natural products and synthetic compounds, including several clinically used chemotherapeutics have been recognized to target TrxR. A number of structurally diversified compounds derived from natural sources have also been found to possess potent inhibitory effect against TrxR. In our laboratory, we had evaluated the possible inhibitory effect of a panel of structurally diversified naturally-occurring compounds and their derivatives on TrxR activity. Sharing in common electrophilic centers, these compounds had been found to possess TrxR inhibitory activity correlating to their antiproliferative activity. On this basis, these compounds can be further developed for applications in cancer chemotherapies that may lead to more desirable clinical outcomes.

INVITED SPEAKER (CANCER DRUG DISCOVERY/ TRANSLATIONAL)
Date: 4th December 2019
Time: 11.20 am - 11.45 pm
Venue: The Ballroom

Can combination with phytochemicals make platinum drugs more desired and welcome?

Assoc. Prof. Dr. Fazlul Huq

The present study aimed to investigate drug action from the combination of platinum drugs and designed complexes with tumour active phytochemicals including curcumin, EGCG, thymoquinone, resveratrol, ursolic acid and genistein in human ovarian tumour models. Activity of the compounds alone and in sequenced combinations in ovarian and colorectal cancer cell lines including A2780, A2780cisR and A2780cisZD0473R were determined using MTT reduction assay. Drug accumulation and drug−DNA binding were determined using established protocols. Proteomic studies involving 2D gel electrophoresis and mass spectrometry were employed to characterize key proteins associated with platinum resistance. Generally but not always sequenced combinations with 2 to 4 h time gap were found to be synergistic. The variation in combined drug action with the change in sequence of administration indicates that the action of one drug is modulated by that of the other. Proteomic studies have identified over thirty proteins believed to be associated with platinum resistance in ovarian cancer. They belong to six major groups including cytoskeletal proteins, molecular chaperone and stress related proteins, proteins involved in detoxification and drug resistance, proteins involved in metabolic processes and mRNA processing proteins. The proteins are restored to normalcy due to treatment with synergistic combinations. If confirmed in vivo, the results suggest that appropriate combinations of targeted therapy and tumour active phytochemicals may provide an effective and affordable means of overcoming drug resistance in ovarian cancer.
PLENARY SPEAKER (CANCER CONTROL AND PREVENTION)
Date: 4th December 2019
Time: 2.10 pm - 2.55 pm
Venue: The Ballroom

Control and Prevention Strategies for Oral Cancer - the Malaysian and Regional Scenario

Prof. Dr. Rosnah binti Mohd Zain

The epidemiology of Oral Cancer is unique and varies from country to country. Its prevalence may differ and in many cases is dependent on the variation of lifestyles and habitual risk factors. Like other cancer research, different aspects of oral cancer research are converging to give an impact on the patients’ quality of life as well as the community. Despite the high volume of literature on oral cancer, patients are still being diagnosed at late stages, especially from the Asian region where almost two-thirds of patients presented with late stage cancers (Stages 3 & 4).

There are two general aspects of oral cancer control strategies which are considered to be of equal importance. One is for those with no cancer where prevention of oral cancer, early detection of oral cancer and prediction of malignant progression are extremely important to reduce the prevalence of oral cancer; whereas for those with oral cancer, effective management strategies can be very challenging due to the heterogeneity of the disease. The search for new strategies and therapeutics in combating oral cancer becomes of utmost importance for curative or palliative intent, which will finally, contributes to improved quality of life of patients.

When considering the Low- and Middle-Income Countries (LMIC), the burden of oral cancer is high and with some countries having inadequate facilities and resources, population-based screening becomes unethical until such a time that the country has enough facilities and human resources to handle the outcome of screening. With this in mind, the move to reduce incidence of oral cancer is to concentrate on efforts on the early detection of oral cancer through public awareness of the disease and the risk behaviors. Prevention through awareness is utmost importance while risk behavior interventions are equally important but may be more challenging to achieve the optimal output.

This presentation will focus on understanding oral cancer (clinicopathologic profiles, risk factors and progression) and their importance in prevention and management strategies in the Malaysian and Regional context.

INVITED SPEAKER (CANCER CONTROL AND PREVENTION)
Date: 4th December 2019
Time: 3.15 pm - 3.40 pm
Venue: The Ballroom

Policy & priorities for National Cancer Control Planning in Low & Middle Income Countries: Lessons from the ASEAN Costs in Oncology, ACTION Study

Assoc. Prof. Dr. Nirmala Bhoo-Pathy

Evidence to guide policymakers in developing affordable and equitable cancer control plans are scarce in low- and middle-income countries (LMIC). The ACTION (ASEAN Costs in Oncology)
study, examined the human cost of cancer to populations across eight countries in Southeast Asia (Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Thailand and Vietnam). The study was designed to assess the impact of cancer on household economic wellbeing and patients’ survival as well as quality of life. In this talk, findings from the overall study, and findings specific to Malaysia will be presented, and the policy implications will be discussed.

INVITED SPEAKER (CANCER CONTROL AND PREVENTION)
Date: 4th December 2019
Time: 3.40 pm - 4.05 pm
Venue: The Ballroom

How much are we shifting paradigms? Impact of Cancer Research in Malaysia

Dr. Murallitharan Munisamy

The word intervention is defined as action taken to intentionally become involved in a difficult situation in order to bring an improvement to it or to prevent it from worsening. Cancer is one of those situations. Across the cancer control continuum spanning from prevention, early detection, diagnosis, treatment and survivorship there are countless issues which continue to impair and impede patients suffering from cancer from obtaining good treatment outcomes. We increasingly know that the etiology of these conditions are multifactorial; and thus proposed solutions need to be from a multisectoral viewpoint as well.

One of the shining beacons of human civilisation thus far has been science and those who work tirelessly to advance its cause: scientists and researchers. From creating new therapeutic solutions to molecular diagnostics we keep on looking for and discovering newer, better weapons in the armamentarium globally to fight cancer. These new solutions and discoveries need to, at the end of the day, be validated through the rigorous methods which make up intervention research; the culmination of a long journey of multiple small scientific discoveries.

Without a doubt, intervention research is the most difficult, critical step between moving from the controlled ‘laboratory’ setting to the ‘real-world’. Rightly so, moving into an intervention phase first requires rigorous planning and methodical stepwise background research before deployment. On the other hand, however, too much caution and a propensity to ‘play safe’ by researchers will continue to limit the amount of interventional research actually being carried out; and thus really making an impact directly on patients especially in the cancer landscape.

Is there a rich, robust scene of interventional research in the local Malaysian landscape in terms of cancer? That is thought-provoking question that needs to be raised and if not, we need to think and act on shifting the paradigm on this, to assist all Malaysians in tackling the cancer burden.
Patient Navigation Program: A New Horizon for Breast Cancer Care

Dato’ Seri Dr. Mohamed Yusof Bin Hj Abdul Wahab

Late stage presentation and poor adherence to treatment protocol remains a major contributor to poor survival for patient with breast cancer in Malaysia. Most women experience psychological distress throughout the course of their journey in battling this disease. It can be related to physical problems like illness or disability, psychological problems, family issues and social concerns such as those related to employment, insurance and supportive care access. Addressing the physical demands of the disease is just one component of the comprehensive treatment regimen for breast cancer; treatment must account for patient’s psychological needs as most of the patient will link cancer with death which results in anxiety and depression.

In Ministry of Health Hospital, breast cancer patients are managed either by the general surgeon or the breast surgeon. In Hospitals where the cases are manage by the general surgeon, the challenge is to offer personalized and dedicated care. Realising this need, in 2004 breast cancer patients presenting to HTAR was manage by a dedicated team (Medical Officer and nurse). Process of care was monitored closely with timeline for both investigation and treatment define. However, the defaulter rate was still high (11.5% in 2014). We realized we needed other initiatives to improve the compliance to treatment.

In 2015, HTAR Surgical Department established a partnership with Cancer Research Malaysia (CRM) and integrated patient navigation program (PN) in the management of breast cancer patient. We named our centre providing patient navigation as Pink Ribbon Centre (PRC). Our aim is to improve the overall compliance of patient to treatment plan. To achieve these, navigators who are qualified nurses in general nursing, oncology and breast care and surgery became part of our management team. Navigators provided patient and family with education tools, supportive care and visit, and practical help in overcoming individual patient barriers. A community navigator from CRM was also placed to address patients’ social welfare needs that hinder completion of cancer care. In addition, the PRC had increased clinic days, dedicated phone lines and implemented an appointment reminder call.

We audited our outcome as regards to timeliness of our work process. Compared to the cohort of patients in the year prior to PN, women with PN received timely mammography (96.4% vs. 74.4%, p<0.001), biopsy (92.5% vs. 76.1%, p=0.003), and communication of news (80.0% vs. 58.5%, p <0.001). PN reduced treatment defaulter rates (4.4% vs. 11.5%, p=0.048). Among navigated patients, late stage at presentation was independently associated with having emotional and language barriers (p=0.01). Finally, the main reason reported for delay, default, or refusal of treatment was the preference for alternative therapy. PN is feasible in addressing barriers to cancer care when integrated with a breast clinic in HTAR. Its implementation resulted in improved diagnostic timeliness and reduced treatment default. Wider adoption of PN could be a key element of cancer control in Malaysia.
Reimagine Medicine – Collaborating to Deliver Innovation

Dr. Balraj Sethi

Cancer is a chapter in history which we will rewrite. We aim to revolutionize cancer care through four major therapeutic area which are Cell & Gene, Immuno-Oncology, Radionuclide and Targeted Treatment. With this four vast therapeutic area we hope to cure and tame debilitating diseases. Whilst we are thriving to bring in more clinical trials to Malaysia to provide access to innovative medicine. In this year alone, Novartis Malaysia has had 16 clinical trials providing access to 182 patients across different therapeutic areas. On our next frontier we are pushing through to do early phase clinical trials in Malaysia. We believe, we can’t transform cancer care alone therefore, we are passionate to collaborate with local research community. Let us reimagine medicine together.
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RSA 1
Tropomyosin Receptor Kinase-C Targeted Dipeptidomimetic Ligand-Drug Conjugates in Photodynamic Cancer Therapy and Immunotherapy

Kue Chin Sian1, Anyanee Kamkaew2, Syed Muhammad Usama3, Lai Phei San1, Kiew Lik Voon4, Chung Lip Yong5, Kevin Burgess3, Lee Hong Boon6

1 Department of Diagnostic and Allied Health Sciences, Faculty of Health and Life Sciences, Management & Science University, Selangor, Malaysia. 2 School of Chemistry, Institute of Science, Suranaree University of Technology, Nakhon Ratchasima, Thailand. 3 Department of Chemistry, Texas A & M University, College Station, USA. 4 Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia. 5 Department of Pharmacy, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia. 6 School of Biosciences, Taylor’s University Lakeside Campus, Subang Jaya, Malaysia.

Background: In spite of intense research, the most commonly used anticancer drugs in the clinic today are still non-specific, killing both cancer and normal cells and compromising immune system, leading to toxicity and even death. An ideal cancer therapeutic are able to overcome the mentioned limitations. Active targeted cancer therapy encompasses strategies wherein a ligand for a cell surface receptor that overexpressed on cancer cells is used to deliver a cytotoxic cargo. Photodynamic therapy (PDT), which utilises the administration of photosensitiser along with focal light activation at specific wavelengths, to generate singlet oxygen species to kill irradiated cancer cells. Tropomyosin receptor kinase-C (TrkC) is being targeted due to its overexpression in cancer including breast, melanoma, pancreatic, neuroblastoma. Methodology: A synthetic bivalent Isoleucine-Yrosine-Isoleucine-Yrosine based TrkC receptor ligand (IY-IY) was designed, and conjugated to a photosensitizer Diodo Boron Dipyromethene (BODIPY), forming IYIY-BODIPY for PDT. For targeted immunotherapy, IYIY-ligand is conjugated to hapten dinitrophenol (DNP) to form IYIY-DNP. The conjugates were studied for specificity, toxicity, efficacy and immunomodulatory in in vitro and in vivo breast murine model. Results: Upon PDT, IYIY-BODIPY at 10 mg/kg induced 71% full tumor remission in TrkC+ 4T1 breast tumor bearing mice, with no metastasis up to 90 days. This observation was neither found in TrkC- 67NR cancer model and scrambled control IYIYI-BODIPY. In addition, the IYIY-BODIPY with PDT had high levels of IFN-γ and IL-17+ T-cell but decreased the levels of immunoregulatory mediators TGF-β, myeloid-derived suppressor cells and regulatory T-cells. Adoptive transfer of immune cells from IYIY-BODIPY-treated survivor mice that were photoirradiated significantly delayed tumor growth (~40–50% smaller size) in recipient mice. For IYIY-DNP in immunotherapy, preliminary data revealed that IYIY-DNP induces clumping of TrkC+ tumor cells with macrophages, then phagocytised, but not in IYIY-DNP and TrkC- cell. Conclusion: IYIY ligand is selective against TrkC, and is a novel ligand for cancer therapeutic.

Keywords: TrkC, photodynamic therapy, immunotherapy, BODIPY, dinitrophenol

RSA 2
Leveraging Machine Learning for Drug Combination Discovery in Pancreatic Adenocarcinoma

Chun-Wai MAI1,2
1Centre for Cancer and Stem Cells Research, Institute for Research Development and Innovation (IRDI), International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, Malaysia. 2School of Pharmacy, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, Malaysia

Pancreatic adenocarcinoma (PDAC) is a highly aggressive cancer with a high chance of recurrence, limited treatment options, and poor prognosis. Our team utilize large scale genomic datasets and computational systems biology to identify potential drugs targeting the PDAC through single and combination therapy. Using the transcriptomic data available from the International Cancer Genome Consortium, Cancer Cell Line Encyclopedia and Connectivity Map, we identified 26 small molecules that could target the squamous subtype of PDAC. Among them include inhibitors targeting the SRC proto-oncogene (SRC) and the mitogen-activated protein kinase kinase 1/2 (MEK1/2) through machine learning. Further analyses demonstrated that the SRC inhibitors (dasatinib and PP2) and MEK1/2 inhibitor (pimasertib) synergized gemcitabine sensitivity specifically in the squamous subtype of PDAC cells (SW1990 and
BxPC3), but not in the PDAC progenitor cells (AsPC1). Further analysis revealed that the synergistic effects are dependent on SRC or MEK1/2 activities, as overexpression of SRC or MEK1/2 completely abrogated the synergistic effects SRC inhibitors (dasatinib and PP2) and MEK1/2 inhibitor (pimasertib). In contrast, no significant toxicity was observed in the MRC5 human lung fibroblast and ARPE-19 human retinal pigment epithelial cells. Together, our findings suggest that combinations of SRC or MEK inhibitors with gemcitabine possess synergistic effects on the squamous subtype of PDAC cells and warrant further investigation. Coupled with our in-house Collaborative Drug Discovery Program (CDD) our steadfast goal remains focused on the discovery of novel therapeutics approaches to improve patient’s lives. Dr Mai will also be sharing his research team’s discovery of hydrazide integrated carbazoles as potential new class of agents targeting PDAC.

RSA 3
Ternary copper (II) complex as Targeted Cancer Agent for Human Breast Cancer Cells

Jhi Biau Foo 1*, Chee Hong Leong 1, Xian Wei Teo 1, Zheng Yang Lee 1, Faris bin Norizan 1, Chun Sing Christopher Wong 1, U Ling Krystal Lim 1, Yin Sim Tor 2, May Lee Low 3, Ng Chew Hee 3

1School of Pharmacy, Faculty of Health & Medical Sciences, Taylor’s University, Subang Jaya, Selangor Darul Ehsan, Malaysia. 2School of Biosciences, Faculty of Health & Medical Sciences, Taylor’s University, Subang Jaya, Selangor Darul Ehsan, Malaysia. 3Department of Pharmaceutical Chemistry, School of Pharmacy, International Medical University, 126, Jln Jalil Perkasa 19, Bukit Jalil, Kuala Lumpur, Malaysia.

BACKGROUND: The use of copper complexes for cancer treatment has been widely explored as cancer cells are reported to take up greater amounts of copper than normal cells. Our group had successfully synthesised and characterised the Cu(phen)(L-tyr)Cl·3H2O copper complex. Nevertheless, the mode of cell death induced by this copper complex against breast cancer cells remains unclear. The current study investigated the mode of cell death induced by Cu(phen)(L-tyr)Cl·3H2O against human breast cancer cells. METHODS: The inhibitory and morphological changes induced by Cu(phen)(L-tyr)Cl·3H2O against human breast cancer cells were determined by MTT assay and inverted light microscopy, respectively. Induction of cell cycle arrest and apoptosis were determined by flow cytometry analysis. The protein expression of p53 and autophagy marker LC3α/β were evaluated by western blot analysis. Results: The growth of cancer cells was inhibited by Cu(phen)(L-tyr)Cl·3H2O in a dose-dependent manner with IC50 value of approximately 3 µM against MCF-7 and MDA-MB-231 breast cancer cells. It was found that Cu(phen)(L-tyr)Cl·3H2O induced S phase cell cycle arrest and apoptosis towards these two cancer cells. The expression of wild-type p53 of MCF-7 cells and mutant p53 of MDA-MB-231 cells was upregulated and downregulated, respectively, suggesting that the induction of apoptosis was via p53 pathway. LC3β was upregulated in both cells upon treatment with Cu(phen)(L-tyr)Cl·3H2O and co-treatment with hydroxychloroquine enhanced the growth inhibition of Cu(phen)(L-tyr)Cl·3H2O towards both cells, suggesting that the induction of autophagy in the breast cancer cells upon treatment with Cu(phen)(L-tyr)Cl·3H2O was for cell survival. CONCLUSION: Our present study provided evidence regarding the anticancer effects and underlying mechanisms of Cu(phen)(L-tyr)Cl·3H2O against human breast cancer cells. These findings shed new light on the potential application of Cu(phen)(L-tyr)Cl·3H2O as targeted anticancer agent.

Keywords: Copper complex, breast cancer, cell cycle, apoptosis, autophagy
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OAK: The Largest Phase III Immunotherapy Study in Previously Treated Advanced NSCLC, Regardless of PD-L1 Expression

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**PFS** programmed death ligand 1
## Oral Session
### Tuesday, 3rd December 2019

### Cancer Biology
**Venue:** PLH3903 classroom  
**CB1. Shivapriya Jeyaraman** - In depth functional analysis of circular RNAs in regulating chemoresistance in FOLFOX resistant colon cancer cells  
**CB2. Karen Ng Lee Peng** - Extracellular prostaglandins E1 and E2 are upregulated in oral premalignant keratinocytes and senescence but differentially regulated by p53  
**CB3. Sweta Raikundalia** - MicroRNA Regulation of Choline Kinase Alpha Gene Expression in MCF7 Breast Cancer Cell Line  
**CB4. Kamariah Ibrahim** - Identification of the Competing Endogenous RNA (CERNA) Network in Human Thymic Epithelial Tumors

### Cancer Drug Discovery I
**Venue:** PLH31005 classroom  
**CD1. Diya Rajasekhar Chinta** - Molecular Modeling of DOT1L protein for the discovery of new potent inhibitors for mixed-lineage leukemia: A molecular docking and ADMET study  
**CD2. Omchit Surien** - Chemoprevention of Lung Squamous Cell Carcinoma with PTEROSTILBENE in Mouse Model  
**CD3. Umi Khalsom Mohd Bajuri** - The Anti-angiogenic Effect of Lactobacillus Plantarum LAB12-Derived Cell Free Supernatant against HCT116 is Associated with Downregulation of VEGF and Upregulation of TSP-1  
**CD4. Sivananthan Manoharan** - Murine Double Minute 2 Inhibitors Induces Cytotoxicity in Nasopharyngeal Carcinoma Cells  
**CD5. Muhammad Azizan Samad** - The Effects of Berberine on Telomerase Activity and Expression of Colorectal Cancer Cell Line, HCT 116

### Clinical Oncology & Cancer Control and Prevention
**Venue:** The Ballroom  
**CO2. Lionel Lian Aun** - Attacking Mutated KRAS Cancers: An Oral Vaccination Approach  
**CO3. Wan Ping Ch'ng** - Treatment Outcome of Nasopharyngeal Carcinoma in the Era of Intensity Modulated Radiotherapy (IMRT) – A single institution experience  
**CO4. Ainon Natrah Aminnudin** - Patient Concerns Inventory (PCI) as an Innovative Approach to Improve Patients’ Quality of Life and Satisfaction During Post-Operative Head and Neck Cancer Consultation Sessions in Malaysia: A Multicentre Study Protocol  
**CO5. Abdelmuniem Siddig Mohamed Ahmed** - Electrocardiogram Changes in Cancer Patients Treated with 5-Flourouracil Chemotherapy at National Cancer Institute- University of Gezira, Sudan

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Wednesday, 4\textsuperscript{th} December 2019

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CB1, P1.1
In Depth Functional Analysis of Circular RNAs in Regulating Chemoresistance in FOLFOX Resistant Colon Cancer Cells

Shivapriya Jeyaraman1, Suzuki Saidin1, Rynia Illani Mohd Yunus1, Muatamurulaini Mustangin2, Azyani Yahaya2, Nurul Syakima Ab Mutalib1, Ezanee Azlina Mohamad Hanif2, Rahman Jamal1, Nadiah Abu1,2

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Background: Colorectal cancer (CRC) is conventionally treated with surgery, and FOLFOX based chemotherapy is widely used as common regimen. However, FOLFOX chemoresistance exists as a hurdle in treating CRC patients. Currently there is no biomarker to predict resistance or desensitize CRC cells towards chemotherapy. Circular RNAs (circRNAs) were found to be a potential player in progression of diseases especially cancer. This study is aimed to determine the circRNAs expression profile in resistant (R) and non-resistant (NR) group to FOLFOX. Methods: Microarray was used to determine the expression of circRNAs in 5 pairs of CRC FOLFOX-R and NR tissue and 3 R and 3 NR HCT116 cells. Bioinformatics analyses were applied to study the differentially expressed circRNAs and miRNA binding sites. qRT-PCR was performed to validate the expression pattern of circRNAs. Results: Using fold change ≥ 1.5 and p < 0.05, our findings revealed that 131 circRNAs were upregulated and 144 downregulated in NR tissue group compared with R tissue group. Whereas, 108 circRNAs were upregulated and 135 downregulated in HCT116 R cell line compared with NR cell line. When data were overlapped, 16 upregulated and 26 downregulated circRNAs were present in both R tissue versus R cell line and NR tissue versus NR cell line. Top 2 upregulated circRNAs, hsa_circ_0024402 and hsa_circ_0007489 and top 2 downregulated circRNAs, hsa_circ_0036592 and hsa_circ_0011385 were selected for validation and were found dysregulated in accordance to microarray results. From bioinformatics prediction tools, hsa_circ_0036592 were predicted to bind to miR-203 and hsa_circ_0007489 to miR-723. These dysregulation suggests a potential role of circRNAs in CRC treatment management. Conclusions: Our findings have produced specific circRNA profiles in FOLFOX treatment resistant group. The aberrantly expressed circRNAs may suggest their involvement in resisting treatments and could serve as a promising biomarker targets for treatment plan in CRC patients.

Keywords: Circular RNA, chemo resistance, circRNA-miRNA interaction, biomarker

CB2, P1.7
Extracellular Prostaglandins E1 and E2 are Upregulated in Oral Premalignant Keratinocytes and Senescence but Differentially Regulated by p53

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Background: Diploid dysplasia (DD) are mortal, genetically stable in-vitro, have low probability of progression to malignancy compared to immortal aneuploid dysplasia (AD). An unbiased metabolomics screen of conditioned medium from confluent cultures in DD showed elevated levels of prostaglandins (PGE1,PGE2) and IL-8 but all are visibly absent in AD keratinocytes. Methods: Conditioned medium from confluent oral keratinocytes was collected over a 24-hour period. Competitive and sandwich ELISA kits were used for detection of PGEs and ILs respectively. p53 knockdown was performed via siRNA. Normal oral keratinocytes and DD were immortalised with ROCK inhibitor (Y-27632) independently of p53 dysfunction. Results: PGEs and ILs were confirmed elevated in DD but not in AD as compared to normal keratinocytes. We also showed keratinocytes rendered immortal by defined disruption of p53 and p16(INK4a) coupled with ectopic telomerase expression (OKF4) and DD cells treated with Y-27632 had reduced, or absent PGE1/2 expression, indicating that one or more mutations involved in keratinocyte immortalisation may regulate PGEs and ILs. Furthermore, one immortal line, OKF6 that differed from OKF4 only in that it had retained wild-type p53 continued to over-express PGEs and ILs, was used as tractable model to study their regulation further. p53 knockdown (80%) in OKF6 reduced PGE1 levels but not PGE2, IL-6 and IL-8 indicating that loss of p53 in AD may only be partially responsible for the regulation of PGEs and ILs. OKF6 was also treated with cyclooxygenase (COX-1,COX-2) and COX2-selective inhibitors and whilst as expected the PGEs were almost eliminated, the ILs remained high showing that OKF6 cells at least, PGEs are not necessary for the high levels of ILs. Conclusion: Over-expression of PGE1, PGE2, IL-6 and IL-8 in DD generally requires an intact senescence programme and functional COX-2 but other unidentified factors are required. Only PGE1 requires p53 once p16(INK4a) is lost.
**CB3, P1.9**

**MicroRNA Regulation of Choline Kinase Alpha Gene Expression in MCF7 Breast Cancer Cell Line**

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**Background:** CKα isoform of Choline kinase enzyme (1st enzyme - CDP-Choline Pathway) has non-catalytic function in tumor onset, progression, cell proliferation and cell signalling. Overexpression of CKα has been observed in human tumor tissues of lung, liver, colon, prostate, breast and ovaries thereby emerging as biomarker for cancer progression and promising target for cancer therapeutics. microRNAs are 18-22 nucleotide long single stranded, evolutionarily conserved small RNAs that function as post-transcriptional regulators of gene expression. microRNAs operate primarily by binding to complementary sequences of 3’ untranslated region (3’UTR) of target mRNA, causing translational repression of target gene expression. Built on this operational principle, the purpose of this research work is to study the effect of in-silico predicted miRNAs on the in-vitro activity of CKα gene expression. **Methods:** microRNAs targeting 3’UTR of CKα were predicted using freely available algorithms. Five promising microRNA transcripts were shortlisted for further analysis: hsa-miR-876-5p, hsa-miR-200a-3p, hsa-miR-141-3p, hsa-miR-367-3p and hsa-miR-32-5p. The synthetic mimics of the shortlisted microRNAs were transfected into MCF7 cell line along with appropriate controls to study their outcome on CKα expression. **Results:** Both, qPCR and Western blot experiments showed a significant downregulation of CKα, mRNA and protein expression respectively, in MCF7 cells transfected with hsa-miR-367-3p, hsa-miR-32-5p and hsa-miR-876-5p, in their order of effectiveness. Percentage of apoptotic cells, counted using Muse Cell Analyzer, also increased in the microRNA treated cells compared to the negative control, with highest percentage in hsa-miR-367-3p transfected MCF7. **Conclusion:** Drawing from the data collected, hsa-miR-367-3p, hsa-miR-32-5p and hsa-miR-876-5p demonstrate a budding outlook in CKα oriented cancer research.

**Keywords:** Cancer, Choline Kinase Alpha (CKα), gene regulation, microRNAs

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**CB4, P1.11**

**Identification of the Competing Endogenous RNA (CERNA) Network in Human Thymic Epithelial Tumors**

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**Background:** Thymomas and thymic carcinoma are two different types of rare tumors commonly classified together as thymic epithelial tumors (TET). Thymomas have the lowest mutational burden amongst adult tumors. Until now, not much is known about the TET biology and its transcriptional regulatory networks. LncRNA, function as competing endogenous RNA (ceRNA) that interact with mRNAs, serving as miRNA sponges to restrain miRNA function by competing for miRNA response element and have role in cancer. We hypothesized ceRNA interactions plays essential role in the development of TET. **Methods:** We utilized 111 TET patients having both miRNA-sequencing and RNA-seq data as well as clinical data from The Cancer Genome Atlas to characterize transcriptional regulatory network using bioinformatics approach. Differentially expressed genes (DEGs) analysis was performed using Limma. DEGs were subsequently uploaded to the network analysis software. LncRNA-miRNA-mRNA interaction network for TET was predicted and constructed using Cytoscape and its associated plug ins. **Results:** We identified 5,000 DEGs from RNA-seq and within the subgroup there were 1,325 DE Incrna. MiRNA-seq analysis revealed 202 DE miRNA. Pathway based enrichment analysis shows that the DEGs involved in the transcriptional misregulation in cancer, hepatitis B and Th17 cell differentiation pathway. We identified several potential hub genes acting as ceRNA using CytoHubba and these genes were validated with GEPIA 2.0. Results for gene expression and Kaplan-Meier survival analysis suggested that identified ceRNA may potentially be used as predictive biomarkers for TET. **Conclusion:** We have identified potential non-coding RNAs that are suggested to be an important regulator in TET pathogenesis. Further in vitro validation needed to be done to confirm functional role of these lncRNA in TET biology.

**Keywords:** thymic epithelial tumors, miRNA, lncRNA, network, ceRNA, thymoma
CD1
Molecular Modeling of DOT1L protein for the discovery of new potent inhibitors for mixed-lineage leukemia: A molecular docking and ADMET study

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Background: Mixed lineage leukemia (MLL) is an aggressive form of leukemia that affects both infants and adults and typically carries a poor prognosis. The underlying genetic defect is a chromosomal translocation that fuses the MLL gene to a variety of partners. Expression of MLL gene results in fusion oncoproteins. These proteins can interact with disruptor of telomeric silencing 1-like (DOT1L) that catalyzes the methylation of histone H3 (H3K79) and leads to leukemic transformation. Inhibition of DOT1L would become an attractive therapeutic target for MLL. Methods: The considerable anticancer activity of pyrazolone was noted from literature and presumed that the derivatives of pyrazolone moeity can be good inhibitors for DOT1L. This study involved virtual screening of 4000 molecules based on structure similarity of pyrazolone from different chemical databases (PubChem, ChemSpider). Molecular docking using Lamarckian Genetic Algorithm on Autodock tool was carried out for these ligands. The top 20 molecules were selected based on the minimum binding energy. The protein-ligand complex was created and visualized using UCSF chimera for H-bond interaction and analysis. Further, shortlisted molecules based on H-bond analysis were evaluated for in-silico ADMET (Absorption, Distribution, Metabolism, Elimination, and Toxicity) predictions and drug-likeness properties. Results: Fourteen ligands with minimum binding energies aligning between -11.18 kcal/mol and -1.25 kcal/mol were shortlisted. They showed intricate intermolecular H-bond formations with active sites PHE 223, ASP 161 and GLU 186 of DOT1L. The drug-likeness scores and ADMET predictions of these shortlisted ligands gave lead to test them for the inhibition DOT1L in-vitro and in-vivo. Conclusion: The shortlisted ligands could be developed as potent drugs to block DOT1L protein and leukemic transformation. However, modifications are recommended in their structures to improve their drug-likeness property and ADMET profiles.

Keywords: PHE 223, ASP 161, GLU 186, Pyrazolone, H-bond analysis, drug-likeness, ADMET

CD2
Chemoprevention of Lung Squamous Cell Carcinoma with PTEROSTILBENE in Mouse Model

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Background: Lung cancer has a high incidence and mortality rate. Squamous cell carcinoma (SCC) of the lungs is one of the most diagnosed types of lung cancer. Pterostilbene (PS) is a potential naturally derived compound that could be developed as a chemopreventive agent due to its antioxidant, anti-inflammatory, and anti-proliferative properties. Thus, this study was conducted to investigate the chemopreventive effect of pterostilbene against lung SCC in mouse model. Methods: Balb/C mice (seven weeks) were randomly divided into four groups (n=6). (1)NTCU group that treated with N-nitroso-trischloroethylurea (NTCU) in 70% acetone topically on shaved subcapsular and corn oil intraperitoneally. (2)Vehicle control (VC) group received acetone and corn oil. Two treatment PS groups: (3)10 mg/kg (PS10) and (4)50 mg/kg (PS50) in corn oil and NTCU. All lungs were harvested after 26 weeks for histopathological analysis, scoring, and measurement of the thickness of epithelium layer. Immunohistochemistry staining of cytokeratin 5/6(CK-5/6) was performed to confirm the lung SCC. Results: Histopathological analysis showed that the PS50 group maintained a normal bronchial epithelium that similar to the VC. PS10 caused hyperplasia of bronchial epithelium layer. NTCU displayed the characteristics of SCC with the formation of keratin pearls and increased nucleus/cytoplasm (N:C) ratio. NTCU has the highest score of 3.7 and VC with the lowest score of 0. PS10 and PS50 scored lower than NTCU with 0.6 and 0.3, respectively. Both PS10 and PS50 significantly reduced the thickness of epithelium layer as compared to the NTCU (p<0.05). The expression of CK-5/6 was higher in the NTCU as compared to the PS10 and PS50; meanwhile no expression of CK-5/6 was detected in VC. Conclusion: Pterostilbene was able to prevent the development of lung SCC. Thus, further investigation is needed to understand the underlying molecular mechanisms of pterostilbene in preventing the formation of lung SCC.
**Keywords:** pterostilbene, histopathology, lung cancer, lung squamous cell carcinoma, cytokeratin 5/6

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**CD3**

**The Anti-angiogenic Effect of Lactobacillus Plantarum LAB12-Derived Cell Free Supernatant against HCT116 is Associated with Downregulation of VEGF and Upregulation of TSP-1**

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**Background:** The limitations of conventional chemotherapy and targeted therapy raise the need for alternative strategies in management of colorectal cancer (CRC). The fact that the majority of CRC are sporadic and associated with diet suggests disease prevention through consumption of probiotics. Probiotics are live good bacteria that confer beneficial effects to their hosts when consumed at optimal amount. There is growing evidence indicating the strain-dependent usefulness of probiotic-derived bioactive metabolites against CRC. As such, the present study examined the anti-angiogenic potential of cell free supernatant (CFS) fermented by unique probiotic lactic acid bacteria (LAB) isolated from locally fermented food *in vitro*. **Methods:** This study first examined the 24-hour differential cytotoxicity of LAB12-derived CFS against HCT116 (human colon carcinoma cell line) and HUVEC (human umbilical vein endothelial cells) by using the Sulforhodamine B Assay. The LAB12-derived CFS was then assessed for its anti-angiogenic potential at the highest subtoxic dose (IC\(_{50}\)) using tube formation assay (for HUVEC) and immunocytochemistry (for HCT116). **Results:** LAB12-derived CFS elicited differential cytotoxicity between HCT116 and HUVEC, with greater selectivity (\(>4\)-fold) towards the former. On the other hand, HUVEC exposed to LAB12-derived CFS formed significantly lesser tube-like structures (\(-62\%; p<0.05\)) even in the presence of pro-angiogenic vascular endothelial growth factor (VEGF). The anti-angiogenic effect of LAB-derived CFS was comparable to that of the positive control, paclitaxel. Immunocytostaining of HCT116 treated with LAB12-derived CFS showed downregulation (\(-47.7\%  16.0\%) of VEGF and upregulation (\(+86.0  8.2\%) of the anti-angiogenic thrombospondin (TSP-1). **Conclusion:** The present findings strongly implied the anti-angiogenic effect of LAB12 against HCT116 and warrants further in depth studies using *in vivo* models.

**Keywords:** angiogenesis, colorectal cancer, probiotics, VEGF, TSP-1

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**CD4**

**Murine Double Minute 2 Inhibitors Induces Cytotoxicity in Nasopharyngeal Carcinoma Cells**

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**Background:** The E3 ubiquitin-protein ligase murine double minute 2 (Mdm2) is a negative regulator of the p53 tumour suppressor gene. Small molecules which disrupt the interaction of p53 with Mdm2 (Mdm2 inhibitors), such as nutlin-3 and idasanutlin, act on the cells with wild type (wt) p53. As the majority of nasopharyngeal carcinoma (NPC) cases harbour wt p53, Mdm2 inhibitors could be useful for the treatment of NPC. **Methods:** NPC cell lines were grown as monolayer cultures while xenograft cells harvested from mice were grown as short-term spheroids. Cell viability was measured using MTS or Cell Titre Glo. Nutlin-3 resistant cells were generated by long-term culture with sublethal increasing doses of nutlin-3. The p53 sequence was determined by PCR-Sanger sequencing. To determine whether nutlin-3 resistance could be due to methylation in the absence of p53 mutation, demethylating agent, decitabine was used. **Results:** Treatment with Mdm2 inhibitor, nutlin-3, resulted in loss of viability of NPC cells. The p53 wild type xenograft spheroids were more sensitive to nutlin-3 compared to the p53 mutant spheroids. Long term treatment of NPC cells with sublethal doses of nutlin-3 resulted in increased resistance of NPC cells towards nutlin-3. The nutlin-3 resistant cells did not harbour p53 mutations. Treatment of NPC cells with decitabine resulted in comparable loss viability of nutlin-3 resistant cells and their parental cells, suggesting that reversal of
methylene does not specifically reverse the resistance mechanism in the nutlin-3 resistant cells. Treatment with idasanutlin (an Mdm2 inhibitor, which is undergoing clinical trials) also resulted in loss of viability of NPC cells. **Conclusion:** Treatment of NPC cells with Mdm2 inhibitors results in the loss of viability of the cells. The mechanism of resistance to Mdm2 inhibitors in our cells is not due to p53 mutations or methylation.

**Keywords:** Mdm2 inhibitors; Nasopharyngeal carcinoma; p53

**CD5, P2.30**

The Effects of Berberine on Telomerase Activity and Expression of Colorectal Cancer Cell Line, HCT 116

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**Background:** Globally, colorectal cancer (CRC) is one of the most common cancer affecting male and female, which has been reported to be associated with increased telomerase expression and activity. Telomerase is the enzyme that functions to maintain the length of telomere which contributes to the unlimited proliferative potential in cancer cells. In this research, two subunits of telomerase are studied, namely human telomerase reverse transcriptase (TERT) and human telomerase RNA component (TERC). **Methods:** Telomerase expression was hypothesized to occur during S phase, hence, colorectal cancer cell line (HCT 116) cell cycle distribution was analyzed at 24, 48 and 72 hours of culture to determine the time-point which has the highest percentage of S phase. Screening of telomerase inhibitors (bولدine, silymarin and berberine) on HCT 116 was done to determine the compound with the lowest concentration that caused 50% inhibition (IC50). TeloTAGGG Telomerase Polymerase Chain of Reaction (PCR) Enzyme Linked Immunosorbent Assay (ELISA) was done to determine the telomerase activity. TERT protein level was determined by western blot. **Results:** The highest S phase percentage occurred at 48 hours. It was revealed that berberine had the lowest IC50. Berberine treatment caused cell cycle arrest indicated by the increment of G0/G1 percentage in berberine-treated HCT 116. Berberine treatment also caused decrement of telomerase activity due to downregulation of TERT protein, as well as TERT and TERC mRNA. Berberine also delayed doubling time but did not significantly affect the relative telomere length of HCT 116. **Conclusion:** In summary, our research suggests that berberine could decrease telomerase activity and expression of HCT 116 which in turn inhibit the proliferative ability of the cells.

**Keywords:** Colorectal cancer, HCT 116, berberine, telomerase, cell cycle

**CO1**

Oral Cancer Patient Management: Adapting Clinical Practice Guidelines to Malaysian Context

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**Background:** Quality of care in every stage of oral cancer management is crucial to achieve optimal cancer outcomes and to improve quality of life of the cancer patients. An evidence-based framework outlining the current and best practices in patient management is essential for oral cancer teams to select the best option of oral cancer care. **Aim:** To adapt clinical practice guidelines for oral cancer management including diagnosis, treatment, and follow-up care, for use by healthcare professionals managing oral cancer patients in Malaysia. **Methods:** The concept of “Guideline Adaptation” was used. Core methodologies included reviewing of high quality evidence and adaptation of recommendations from existing guidelines, blended with expert judgements. The Practice Guideline Evaluation and Adaptation Cycle (PGEAC) consisted of six steps namely clinical areas to promote best practice; literature search to identify existing guidelines; guideline assessment in terms of quality, currency, and content; adopting or adapting guidelines for local use; seeking multidisciplinary specialists’ feedback and finalising. **Results:** Fifteen potential existing guidelines were selected through systematic literature search. Only three were considered most appropriate for adaptation to the local context namely the National Comprehensive Cancer Network (2015), Belgian Healthcare Knowledge Centre (2014) and Scottish Intercollegiate Guideline Network (2006) based on good performance in the quality assessment using the Appraisal of Guidelines for Research and Evaluation (AGREE II)
Attacking mutated KRAS cancers: An oral vaccination approach

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Background: Codons 12/13 somatic point mutations of the KRAS gene coding for GTPases downstream of receptor tyrosine kinases is the predominant mutated isofrom (~86%) amongst RAS family members. At present, monoclonal antibody therapies such as cetuximab and panitumumab have proven ineffective against EGFR(+)KRAS(+) neoplasms, while other non-specific chemotherapeutic regimes such as FOLFOX and FOLFIRI are often accompanied by negative side effects and mortality-associated risks with poor outcome. Treatment efforts are currently shifting towards immunotherapeutic approaches, of which next generation engineered peptide cancer vaccines known as mimotopes are rapidly gaining momentum. Methods: In this study, the design and evaluation of orally-administered modified G12V and G12A mutated K-ras peptide vaccine candidates were reported. Sequence modifications of G12V/G12A epitopes were simulated in silico using the IEDB server, synthesized and cloned into pNZ8048 lactococcal vectors. A double-coated mucoadhesive film approach containing live recombinant lactococcal cells was developed, and orally administered to Balb/c mice over a 3-booster immunization schedule. Results: The double-coated mucoadhesive film containing live recombinant lactococcal cells was successful in significantly enhancing upper gastrointestinal survivability by 3.5 folds compared to unprotected controls, thus providing superior bioavailability and efficacy. In vivo immunization data demonstrated that the engineered G12V mimotope candidate with enhanced antigenicity, solubility and MHC-restriction properties were capable of inducing Th2-bias cytokine responses followed by the production of anti-G12V K-ras IgG and IgA in immunized mice sera. Meanwhile, sequence modifications made on the G12A mimotope candidate indicated successful and improved activation of a Th1 cell-based response as indicated via immunophenotyping and IFN-γ ELISPOT data when compared to unmodified epitope controls. Conclusion: This study indicates that non-antigenic cancer self-antigens can be engineered into potentially immunogenic cancer antigens for immunotherapeutic interventions. Challenge studies in xenografted humanized mice are currently underway in assessing the prophylactic and therapeutic efficacy of this vaccine against various KRAS positive malignancies.

Keywords: KRAS, vaccine, colorectal cancer, immunotherapy, Lactococcus lactis
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CO3, P4.1
Treatment outcome of nasopharyngeal carcinoma in the era of Intensity Modulated Radiotherapy (IMRT) – A single institution experience

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Background: Nasopharyngeal carcinoma (NPC) is endemic in South East Asia. Radiotherapy (RT) with or without concurrent chemotherapy (CRT) remains the mainstay of treatment. The Malaysian National Cancer Institute (NCI) is a tertiary public institution established 5 years ago. This study aims to analyse the treatment outcomes in patients with localized NPC treated with IMRT in our institution. Methods: All newly diagnosed, histologically confirmed locally advanced NPC patients (Stage I–IVB) from September 2013- April 2018 who received radiotherapy to faciocervical 70Gy/35F/7weeks with IMRT technique were identified from internal database. Staging was based on 7th AJCC Staging (2010).Histopathological confirmation was based on WHO classification. Some patients (high risk)
received induction chemotherapy (2-3 cycles) prior to RT. Most patients received weekly CRT. The date of local recurrence and distant metastasis were acquired. However, 66 patients have not been assessed radiologically for local recurrence/metastasis at point of cut off. Data collected were analysed using ‘R’ version 3.5.3. Results: 277 patients were identified in the study. Median follow up was 32.3 months. The majority (75.8%) were Stage III and IV at presentation. This contributed to why induction chemotherapy was given in majority of the cohort (62.1%). CRT with IMRT was a favourable prognostic factor for OS (p<0.001) and PFS(p=0.002). The 3-year PFS and OS rates were 66.6% (95%CI 60.1;72.3) and 77% (95%CI71.1;81.9) respectively. Local control rate was 85.3-88.9% in 3 years. 12 and 29 patients had local recurrence and distant metastasis respectively. 19 had both local and distant failure. Conclusion: IMRT is effective in achieving good loco-regional control. Distant metastasis is the commonest site of failure. CRT improves PFS and OS. A longer follow-up is required as median OS and PFS has not been reached in this cohort.

Keywords: Intensity modulated radiotherapy, nasopharyngeal carcinoma, overall survival, progression free

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CO4 Patient Concerns Inventory (PCI) as an Innovative Approach to Improve Patients’ Quality of Life and Satisfaction During Post-Operative Head and Neck Cancer Consultation Sessions in Malaysia: A Multicentre Study Protocol

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Background: Oral cancer and its treatment undisputedly impacts patients’ quality of life, posing a challenge to clinicians in managing them optimally. Identifying patients’ QOL issues is central to total patient care; as such time constraints faced by clinicians during consultation sessions may pose a barrier in identifying such concerns effectively. In this aspect, the use of PCI-H&N during post-op oral cancer consultation sessions has previously shown to be beneficial, simultaneously promoting effective doctor-patient communication during consultations. Objectives: This study intervention is aimed to improve patients’ quality of life and satisfaction with the consultation, and further assess its usefulness, feasibility and the computerised web-based version of PCI-H&N as a new approach at Oral Maxillo-Facial Surgery (OMFS) Clinics, Malaysia. Methods: This protocol describes a comparative study of parallel randomised control trials among post-op oral cancer patients in six OMFS Clinics in Government Hospitals, Malaysia. Eligible patients of 1 month until 5 years follow-up will be randomly assigned into 3 groups (required sample size: 64 per arm; total=192) of paper version of PCI, computerised web-based of PCI and control group. A self-administered questionnaires will be administered with assistance from researcher or their proxies. The primary outcomes are patients’ quality of life represented in the FACT-H&Nv4.0 and patients’ satisfaction with the consultation session measured by a study specific questionnaire. Patients’ psychological distress, feasibility and preferred versions of PCI-H&N are secondary outcomes assessed by using DT score and study specific questionnaires respectively. The outcomes will be analysed using Chi-square test, t-test and linear regression, and expected to be completed by May 2020. Discussion: This study could potentially enhance patient-centered care by improving doctor-patient communication, identifying oral cancer patients’ concerns and further improving quality care delivery for Malaysian oral cancer patients. In addition, the computerized web-based version is in tandem with patient health management system advancement.

Study registration: NMRR-18-3624-45010 (IIR); Funding: Self-sponsored

Keywords: Patient Concerns Inventory (PCI), quality of life, post-op oral cancer patients, web-based computerised, consultation.

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CO5
Electrocardiogram Changes in Cancer Patients Treated with 5-Flurouracil Chemotherapy at National Cancer Institute- University of Gezira, Sudan

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Background: 5-fluorouracil (5-FU) is a key chemotherapeutic agent in the treatment of many gastrointestinal tract adenocarcinomas. Despite its proven therapeutic efficacy, 5-FU also possesses several undesired cardiac toxicities. Including coronary vasospasm, coronary thrombosis, cardiomyopathy and sudden cardiac death. Methods: This is a prospective, cross-sectional and analytical hospital-based study, which was conducted to assess Electrocardiogram changes in cancer patients, who were treated with 5-fluorouracil chemotherapy at national Cancer institute-university of Gezira in the period between September to December in 2018. A structured questionnaire was designed. Then twelve-lead ECG was recorded before, and 24 hours after the beginning of the administration of chemotherapy of 5FU. Results: The study showed that ECG records changed post 5 FU in 29% of the patients. The pattern of ECG changes were as following: 4% of the patients have left axis deviation, 5% have right bundle branch block, 3% have inverted T wave, 5% had corrected QT interval between 0. 471-0.50 second and 3% more than 0.50 second respectively. Moreover: 2% of them developed left ventricular hypertrophy and 7% have a low voltage compared with normal ECG records before taking of 5FU. However, the study does not show any change in rhythm or ST segment. Also, the study found that no relation between the mode of administration of the drug and ECG changes. However; there was a relation between number of cycles and the heart rate after the treatment and there was a strong relation between number of cycles and T wave inversion after the treatment. Conclusion: The study concludes that the 5-flourouracil chemotherapy cause electrocardiogram changes as an indicator of cardiotoxic effect of the drug.

Keywords: 5-flurouracil; Cardiotoxicity; Chemotherapy; Electrocardiogram

CD6, P2.4
In Vitro Study on Cytotoxic and Antioxidant Activity of Morinda Citrifolia (Noni) Juice Deodorized with Weak Base Ion Exchange Resin

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Background: Most consumers avoid consuming noni juice due to its undesirable odour caused by medium chain fatty acid such as octanoic acid. Deodorization was done to remove the octanoic acid using deacidification process by weak ion exchange resin. Several studies have suggested that noni fruit extract has potential in anticancer affect and is high in phytochemical compounds. Thus, this study was conducted to determine the anticancer properties of deodorized noni juice toward breast cancer cell line (MCF-7). Methods: Deodorized noni juice and original noni juice of different concentration were tested on MCF-7 for cell viability. The antioxidant activity, FTIR spectrum analysis and quantification of alizarin using HPLC-PDA of deodorized and original noni juice were carried out. Results: Both deodorized and original noni juice showed a weak cytotoxic activity toward cell line MCF-7 with IC50 values of more than 1000 ppm. The antioxidant activity (DPPH and FRAP) of original noni juice is higher than deodorized noni juice. In FTIR spectrum analysis, both deodorized and original noni juice showed similar spectra trend. Alizarin, quantified by HPLC-PDA, were higher in original juice than in deodorized juice. Conclusion: In conclusion, deodorized noni juice showed similar cytotoxic activity with original noni juice, despite having lower antioxidant activity and alizarin content than original noni juice.

Keywords: Morinda citrifolia, anticancer, deodorized, weak base ion exchange resin
CD7, P2.5
Ternary Copper (II) Complex Induced Cell Death Mechanism on HT-29 Colorectal Cancer Cell Line
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Background: Colorectal cancer patients are commonly treated using chemotherapeutic drugs including platinum complexes, which kills cancer cells by DNA disruption. However, platinum-based drugs are non-selective and increasing drug resistance were reported. This triggers the search for alternative metallic compounds with improved anti-cancer properties. As an alternative, copper restricts multiple aspects of cancer advancement. Cancer cells are reported to uptake more copper than normal cells. Therefore, this study investigates the anti-cancer properties of copper complexes on HT-29 colorectal cancer cell line. Methods: Anti-proliferative activity of Cu(SBCM)2 and Cu(phen)(L-tyr)Cl·3H2O was tested by MTT and real time cell monitoring analysis. Cell cycle analysis and Annexin-V/PI assay were carried out to investigate the induction of cell cycle arrest and apoptosis in treated HT-29 cells. Mitochondrial dependent pathway of copper complex was tested by JC-10 assay. Induction of oxidative stress by copper complex was assessed by ROS assay. Lastly, western blot was done to test the involvement of caspase-8, caspase-9 and p53 in copper complex-treated cells. Results: HT-29 cell growth were inhibited by Cu(phen)(L-tyr)Cl·3H2O in a dose-dependent manner with IC50 value of 2.35 ± 0.35 μM. At 48 hours, the inhibition concentration was over 30 folds lower than of cisplatin. It was found that Cu(phen)(L-tyr)Cl·3H2O induced S-phase cell cycle arrest on HT-29 cells, therefore inducing apoptosis. Mitochondrial membrane potential was not affected by copper complex, therefore no ROS production observed. This was supported by western blot analysis where HT-29 cells were observed to undergo extrinsic apoptotic pathway by upregulated caspase-8 cleavage and downregulated of p53. Conclusion: Our current study elucidates the evidence of anticancer effects and underlying mechanism of Cu(phen)(L-tyr)Cl·3H2O against human colorectal cancer cells. These findings shed a new light on the potential application of Cu(phen)(L-tyr)Cl·3H2O as an anticancer agent.

Keywords: Copper complex, Colorectal cancer, Anticancer, Cell death mechanism

CD8, P2.8
SRS07-Induced Akt Hyperactivation Associated with Reactive Oxygen Species Production Renders Pancreatic Cancer Cell Death
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Background: Over 90% of pancreatic ductal adenocarcinoma (PDAC) tumours harbour driver mutations in K-Ras, which activate various downstream effector-signalling pathways, including phosphoinositide 3-kinase (PI3K) pathway that governs cellular growth and survival. Our previous analysis had identified an andrographolide (AGP) derivative, SRS07, bound to oncogenic K-Ras and abrogated its function. SRS07, an acetylated analogue of SRJ09 had displayed tremendous improvement anticancer activity against various cancer cell lines. This study was aimed at investigating the effect of SRS07 on Ras-dependent PI3K signalling in PDAC cell lines. Methods: The anti-proliferative activity of SRS07 against PDAC cell lines harbouring wild-type (BxPC-3) or mutant K-Ras (PANC-1 – K-RasG12D; Capan-2 – K-RasG12V; MiaPaCa-2 – K-RasG12C) was determined using MTT assay. Western blot analysis was performed to assess the activation of K-Ras through GTP-loading assay, and to identify the change in activity or expression of PI3K cascade-related proteins (PI3K, Akt, PDK1, mTOR, and PTEN) upon treatment with SRS07. Measurement of intracellular reactive oxygen species (ROS) was determined using the 2′,7’-dichlorodihydrofluorescein diacetate (DCF-DA) staining approach. Results: SRS07 was selective towards Capan-2 cells and presented almost 10 times higher potency (mean IC50 = 2.3±1.5 µM) in comparison with SRJ09 (mean IC50 = 25.5±5.6 µM). Upon treatment of SRJ09 and SRS07 at 10 µM, SRS07 showed greater repression in GTP-loading of K-Ras and suppressed the phosphorylation of PI3K p85 regulatory unit in Capan-2 cells. The expression of PDK1, which activates Akt, was significantly reduced. However, a strong Akt activation was observed in Capan-2 cells after 24-hr treatment with SRS07. The compound induced formation of ROS in a time- and dose-dependent manner in Capan-2 cells. Conclusion: SRS07 likely binds oncogenic K-Ras and activates Akt, leading to ROS-mediated apoptosis in Capan-2 cells via a non-canonical inhibition of PI3K signalling pathway.
**CD9**

Bioprospecting of Malaysian Plant Species towards Identification of Potential Anti-cancer Agents

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**Background:** Cancer prevalence ranges from 0.4% to 5% in each population around the world and it was estimated that 100 million out of 7.7 billion people across the globe had cancer (any forms) in 2017. Cancer mortality is also expected to increase in the next decade. Malaysia, one of the megadiversity countries, has an estimated of 15,000 plant species which may offer a great source of therapeutic agents including cancer. As part of the effort in discovery of plant-based anti-cancer agents, FRIM has started to screen a series of extracts against ovarian, breast and colorectal cancer cell lines since 2004 for identification of active anti-proliferative compounds. **Methods:** At least three different plant parts from fifteen plant species were selected and subjecting these samples to solvent or aqueous extraction procedure. Sulfur-homadine B (SRB) assay was used to evaluate the anti-proliferative effects of these plant extracts. The most potent extracts were subjected to chemical isolation of active compounds. Upon characterization via NMR and LCMS, active compounds would be upscaled and further evaluated for in vivo toxicity and modes of action via proteomics and in silico approaches. **Results:** Thus far, more than 763 extracts from 317 species had been screened against the respective cancer cell lines. Active compounds identified through the screening programme include 17βH-nerifolin and 9-methoxycanthin-6-one, with their IC50 ranged from 10 nM to 8 µM. These compounds were found to target Na+/K+-ATPase and fifteen differentially expressed proteins (including AL1A1, KPYM, ANXA2). Based on Lipinski’s rule of five, these compounds were found to be druggable. The LD50 of 9-methoxycanthin-6-one and 17βH-nerifolin were > 300-2000 mg/kg body and > 5-50 mg/kg body weight of female ICR mice, respectively. **Conclusion:** The active compounds will be subjected to pharmacokinetics and sub-chronic in vivo studies to identify a go/no go steps towards pre-clinical and clinical studies.

**Keywords:** plant extracts, Sulfur-homadine B assay, proteomics, in vivo toxicity, in silico

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**CD10, P2.17**

Symmetric Molecules With 1,4-Triazole Moieties As Potent Inhibitors Of Tumour-Associated Lactate Dehydrogenase-A

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A series of symmetric twenty molecules incorporating aryl or pyridyl moieties as central core and 1,4-substituted triazoles as a side bridge was synthesized adopting the click chemistry approach. The new compounds were investigated as lactate dehydrogenase (LDH, EC 1.1.1.27) inhibitors. All the test compounds were found to be good inhibitors for the enzyme with varying percentage of enzyme inhibition ranging from 63-94% as compared to the standard drug (Galloflavin) which exhibited 73.88% enzyme inhibition. The cancer associated Lactate Dehydrogenase-A (LDH-A) isoform was inhibited with the IC50 values from 117 to 174 µM. Seven compounds exhibited better LDHA inhibition (IC50: 117–136 µM) as compared to the known LDH inhibitor – galloflavin (IC50: 157 µM).

**Keywords:** Lactate dehydrogenase; Inhibitors; Triazole
CD11, P2.28

ANTI-CANCER ACTIVITIES OF SEMI-PURE FRACTION ISOLATE FROM ELEUSINE INDICA MEDICINAL PLANT COLLECTED IN KOTA KINABALU, SABAH

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Background: Cancer incidence is rapidly growing worldwide, including Malaysia. The major obstacle to cancer treatment is the recurrence of tumour and the side effects of chemotherapy drugs. Therefore, new anti-cancer drugs and therapies need to be developed urgently. Herbal medicines, which are long used to treat various diseases, are likely to produce lesser side effects than synthetic drugs. E. indica (Poaceae) is medicinal plant used by the natives of Sabah, Malaysia to treat food poisoning, tonic and several other ailments. However, limited studies have been done to examine the effect of the plant extracts on cancer cells. Therefore, this research aims to assess the cytotoxic and apoptotic effects of the extracts and fractions isolate from E. indica toward colorectal cancer (CT26) and breast cancer (MCF-7). Methods: Extracts and fractions were isolated from E. indica via modified Bligh and Dyer extraction protocol. The anti-cancer potential extracts were screened against the colorectal cancer (CT26) and breast cancer (MCF-7) by colourimetric assay and its cell death triggering mechanisms using mass spectrometry-based metabolomics. Results: The most effective crude extract was further purified using chromatography technique. Eight fractions were acquired, and each fraction was tested against the cancer cells at different concentrations (10, 25, 50 and 100 μg/mL). Chemometric analysis revealed the metabolites between treated and non-treated cancer cell by semi-pure fraction were significantly (p-value < 0.05) perturbed. These metabolites were found to have correlation to the programmed cell death. Conclusion: To conclude, semi-pure fraction isolate from E. indica has cytotoxicity effect towards colorectal cancer (CT26) and breast cancer (MCF-7).

Keywords: E. indica, metabolomics, colorectal cancer (CT26), breast cancer (MCF-7)
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TCL.P3.1


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Background: MicroRNAs (miRNAs) are a group of single strand RNAs of about 19-23 nucleotides. MiRNAs control posttranscriptional regulation of gene expression in a broad range of biological system, thus have huge potential as biomarkers for early detection of cancer. According to the Malaysia national cancer registry report, breast cancer was the most common cancer in Malaysia, with 43% of the patients presented at stage III and IV. Recent Malaysian study on cancer survival indicated that the 5-year relative survival of Malaysian breast cancer patients ranged from 87.5% at Stage I to 23.3% at Stage IV. Methods: In this study, plasma miRNA profiles of 8 early stage breast cancer patients and 9 age-matched (± 2 years) healthy controls were characterized by high-throughput quantitative RT-PCR, followed by differential gene expression analysis and construction of Receiver Operating Characteristic (ROC) curve to determine the capability of the assays to discriminate between breast cancer and the healthy control. Result: Among 372 human miRNAs that were analyzed, 40 miRNAs were significantly ≥ 2 fold change between breast cancer patients and controls, with 24 miRNAs being upregulated and 16 miRNAs being downregulated. ROC curve analysis revealed that 8 miRNAs (miR-27b-3p, miR-22-5p, miR-145-5p, miR-181c-5p, miR-423-5p, miR-193a-5p, miR-142-3p, and miR-125b-5p) had area under curve (AUC) value > 0.7 (AUC, P < 0.05). Overlapping findings from ROC analysis and differential gene expression analysis resulted in three miRNAs (miR-27b-3p, miR-22-5p, miR-145-5p). The Cohen’s effect size for these three miRNAs were large with d value more than 0.95. Conclusion: miR-27b-3p, miR-22-5p, miR-145-5p, miR-181c-5p, miR-423-5p, miR-193a-5p, miR-142-3p and miR-125b-5p could be potential...
biomarkers to distinguish breast cancer patients from healthy controls. Validation study for these 8 miRNAs in an external set of samples are ongoing.

**Key words:** Breast cancer, microRNA, biomarkers, early detection, HUSM

**TC2, P3.2**

**Immunoprofile from Blood Circulation and Tumour Microenvironment of Mouse Bearing Breast Cancer Model Post-Irradiation Therapy**

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**Background:** Current studies have reported that radiotherapy-induced immune changes in the tumour microenvironment (TME) that might be responsible for either pro- or anti-tumorigenic activity. However, the mechanism of this effect is still unclear. Hence, little is known about the correlation between the circulating immune cells with that presence in the TME after radiation exposure. The objective of the study to investigate the effect of gamma-ray irradiation on immune cells focusing on eosinophils in EMT6 mouse bearing tumour model at acute stage 96 hrs post-irradiation. **Method:** A total of 24 BALB/c mice aged between 6-8 weeks were divided into 4 groups (n=6), with 3 groups with each mouse were inoculated with 1x 10^6 EMT 6 cells at their left hind leg and one group serve as negative control. On day-8 post-inoculation, 2 groups were received gamma irradiation with absorbed dose 2 Gy and 8 Gy and another served as sham control. At 96 hrs post-radiation, cardiac puncture was performed for blood analysis and tumour sample was collected for flowcytometry analysis. The derived single cell suspensions were incubated with several antibodies for identification of different immune cells. **Results:** Results showed that there was a significant difference only in eosinophil percentage in TME between mice irradiated with 8 Gy (5.60±2.59 %) compared with sham (1.07±0.47 %) and mice irradiated with 2 Gy (2.03±1.29 %). Meanwhile in blood analysis, irradiated group of mice showed total WBC for both dose 2 Gy (2.35±0.34 x10^3µL) and 8 Gy (0.68±0.21 x 10^3µL) has shown significant immunosuppression effect compared to sham (6.75±2.23 x 10^3µL) and healthy (6.96±3.12 x 10^3µL) mice. In term of differential WBC count, lymphocyte and basophils have shown significant difference across the group. **Conclusion:** In conclusion radiation thus induced immune changes not only in the circulation but also at the TME. Further investigation is needed to understand this implication towards the tumorigenic activity.

**Keywords:** mouse bearing tumour model, radiotherapy, tumour microenvironment, white blood cell

**TC3**

**PD-L1 and Akt as the Next Therapeutic Targets for the Triple Negative Breast Cancer using in vitro Study and Transcriptomic Data Analysis**

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**Background:** Triple negative breast cancer (TNBC) is a diverse and the most incurable kind of breast tumors. It lacks estrogen and progesterone receptors and HER2 expression. The TNBC cells do not respond to conventional hormone therapy and anti-Her2 therapy. Therefore, tyrosine kinase inhibitors (TKIs) (such as lapatinib) in combination with immune checkpoint inhibitors (such as anti-PD-L1s) are now seen as promising therapy against TNBCs. This research discusses Akt and S-phase kinase-associated protein 2 (Skp2) as well as PD-L1 and CD86 as possible therapeutic targets for TNBC. **Methods:** To study the mechanism of resistance to lapatinib, the kinase activity of p38, ERK1/2, EGFR, and AKT using ELISA and western blotting in MDA-MB231 (TNBC) and MCF-7 (as control) cell lines. The expressions of EGFR, Akt, Skp2, PD-L1 and CD86 obtained from Cancer Cell Line Encyclopedia (CCLE) were analyzed in 10 TNBC cell lines. Additionally, in order to find better targets for TNBC, clinical data of TNBC (N=116) and breast cancer (N= 1095) patients were obtained from the Cancer Genome Atlas (TCGA), and then the expressions of EGFR, Akt, Skp2, HDAC-9, Gonadotropin-releasing hormone receptor (GNRHR), CD28, CD86, and PD-L1 were compared. **Results:** Lapatinib enhanced the level of p-Akt in MDA-MB231 cell. Using transcriptomic data, TNBC cells expressed Skp2 and Akt more than in EGFR. In addition, TNBC cases had a strong expression of PD-L1, CD28, and CD86. However, average quantities of PD-L1 and CD86 expressions were higher than those in breast cancer cases. In TNBC, the average of Skp2 expression was also higher. Analysis showed only CD86 expression was higher.
significantly correlated to survival rate of TNBC patients. **Conclusion:** Akt in combination with PD-L1 and CTLA-4 appear to be a promising therapeutic target for TKI-resistant TNBC cells.

**Keywords:** Breast cancer, TNBC, Akt, PD-L1, immunotherapy, therapeutic targets

**TC4**

**Synthesis, Characterization and Formulation of PEGylated Glycol Chitosan-based Nanoparticles for Hydrophobic Drug Delivery**

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**Background:** Drug nanoparticles can improve the delivery of hydrophobic chemotherapeutic drugs in the body. Glycol chitosan (GC) is a water-soluble chitosan derivative that can be modified into a polymeric vehicle for the drug nanoparticle formulations. Itraconazole (ITZ) is a potential hydrophobic drug for repurposing into a chemotherapeutic agent for its well-known pharmacokinetic and toxicological profiles. The aim of the study is to synthesise and characterise palmitoylated glycol chitosan polymer grafted with polyethylene glycol (PEG) and to formulate the polymer with ITZ into a stable nanoparticle formulation. **Methods:** GC was degraded and attached with PEG (PEGylation) to form GC-PEG at either room temperature (RT) or 50ºC reactions. Later, different ratios of palmitic acid N-hydroxysuccinimide (PNS) were used to form palmitoylated GC-PEG (PGC-PEG). The product of each step was confirmed using proton nuclear magnetic resonance (¹H-NMR) and Fourier-transform infrared (FTIR) spectroscopy. ITZ and PGC-PEG were formulated into nanoparticles in the form of either polymeric micelles or nanoemulsion at drug to polymer ratio of 1:10. Each form of nanoparticles were subjected for the physicochemical characterization. **Results:** The degree of PEGylation was 4.2% for the reaction at 50ºC compared to 3.3% for reaction at RT. The degree of palmitoylation was 60% and 34% when 792 mg and 396 mg of PNS used, respectively. FTIR analysis confirmed the PEGylation of the GC by assessing the attachment of the succinimidyl group to the amino group on the GC backbone. The polymeric micelles showed average particle size of 291 nm with 39.6% drug encapsulation, whereas nanoemulsion at the size of 400 nm had 80.4% drug encapsulation. **Conclusion:** The stepwise synthesis protocol was able to produce PEGylated GC-based polymer that can be used to produce drug nanoparticles for the delivery of hydrophobic drugs. Future work will involve characterization of the nanoparticle formulations in in-vitro and in-vivo model.

**Keywords:** Glycol chitosan, PEGylation, palmitoylation, itraconazole, drug delivery

**TC5**

**Isocitrate Dehydrogenase mutations in Patients with liver cell plasticity and biliary cancer Admitted to Khartoum Oncology Hospital, Khartoum State – Sudan**

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**Objective:** Intrahepatic cholangiocarcinoma (ICC) is an aggressive cancer associated with the bile ducts within the liver. Mutant IDH acts through a novel mechanism of oncogenesis producing high levels of the metabolite 2-hydroxyglutarate which interferes with the function of α-ketoglutarate-dependent enzymes that regulate diverse cellular processes including histone demethylation and DNA modification. This study aimed to determined the presence of mutations in the isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) genes in Patients with liver cell plasticity and biliary cancer Admitted to Khartoum Oncology Hospital, Khartoum State – Sudan **Result:** By use in vitro stem cell systems and genetically engineered mouse models (GEMMs) to demonstrate the mutant IDH which promotes ICC formation by blocking hepatocyte differentiation and increasing pools of hepatic progenitors that are susceptible to additional oncogenic hits leading to ICC. They found that silencing of HNF4A—encoding a master transcriptional regulator of hepatocyte identity and quiescence—was critical to mutant IDH-mediated inhibition of liver differentiation. In line with these findings, human ICC with IDH mutations are characterized by a hepatic progenitor cell transcriptional signature suggesting that they are a distinct ICC subtype as compared to IDH wild type tumors. The role of mutant IDH in controlling hepatic differentiation state suggests the potential of newly developed inhibitors of the mutant enzyme as a form of differentiation therapy in a solid tumor.

**Keywords:** IDH, mouse models, Cholangiocarcinoma, Khartoum State
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The Effects of Chemotherapy-induced Extracellular Vesicles (Chemo-EVs) on CD8 T Cells

Nur' Syahada Ab Razak, Norahayu Othman, Siti Nurmi Nasir, Zairul Azwan Mohd Azman, Nurul Syakima Ab Mutalib, Mohamad Aimanuddin Mohtar & Nadiah Abu

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Background: Oxaliplatin-based treatment (FOLFOX or XELOX) are utilized as colorectal cancer (CRC) chemotherapeutics in clinical oncology. These chemo drugs are genotoxic agents that alters the DNA of cancer cells and inhibit cell division and growth. There are ample preclinical studies have shown the fraction of DNA damage agent could promote immunogenic cell death and alter the inflammatory milieu of the tumor. Extracellular vesicles (EVs) may interact with tumor microenvironment and interfere the anti-tumor functions especially related to tumor immunity. However, there is a pressing need to deeply understand the role of chemotherapy on EVs and its effects on the immune system. Therefore, we attempt to determine the immunomodulatory effects of chemotherapy-induced-EVs derived from colorectal cancer patients on CD8 effector T cells.

Methods: Extracellular vesicles (EVs) were isolated from the serum of 37 patients of CRC undergoing chemotherapy (Chemo-EVs) and 22 patients of CRC not undergoing chemotherapy (non-induced EVs). Morphology, quantity and physical properties of the EVs were characterized. The coculture assays between EVs and activated CD8 T cells were performed to investigate the functional effects of EVs on immune cells.

Results: The morphology, quantity and physical properties of Chemo-EVs were slightly different than the non-induced EVs. The Chemo-EVs induced the apoptosis of CD8+ T cells and suppressed the ability of CD8+ T cells proliferation as compared to the non-induced EVs. Moreover, the cytokines of the immune cells upon stimulation by Chemo-EVs were differentially expressed.

Conclusions: Chemo-EVs carry molecules that may interfere with the functions of CD8+ T cells. Further study is needed to understand the roles of chemo-EVs in relation with other immune cells as well.

Keywords: Extracellular vesicles, immune cells, therapy, cancer

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Protein Protein Network Analysis and Identification of Key Hub Genes in Oesophageal Cancer

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Background: Oesophageal cancer occurs when uncontrolled growth of abnormal cells in the food tube (oesophagus). Oesophageal cancer is one of the most prevalent malignant tumors in the food tract with worldwide distribution due to late clinical development, rapid growth and very poor survival. In addition, the reason for this poor prognosis is that oesophageal cancer normally indicates widespread local tumor invasion and frequent spread to metastatic locations, especially regional lymph nodes. The spread of malignant tumors is therefore a multi-step technique and many stages of tumor invasion require degradation or breakdown of the extracellular matrix and connective tissue around tumor cells. The objective of this study is to analyse all genes involved in protein-protein interaction through systems biology approach and to identify key genes involved in Oesophageal cancer.

Methods: There is a total of 108 genes which causes oesophageal cancer and protein-protein network was constructed and analyzed using these genes. The genes are obtained from UniProt database using STRING and Cytoscape 3.7.1 tools. Moreover, the functional enrichment analysis was done to identify the key genes by using CentiScape and FUNRICH database.

Results: RBM8A, ZWINT, EIF4A3, BRCA2, GNB2L1 were recognized as the main genes in the network based on network topology parameters. Among them, EIF4A3 gene with the greatest betweenness centrality and node degree was acquired as a super hub gene. The assessment of functional enrichment was carried out using the FUNRICH database.

Conclusion: From this study, Eukaryotic initiation factor 4A-3 (EIF4A3) identified as one of key genes in...
Oesophageal cancer. This result suggests the potential role for EIF4A3 to serve as a diagnostic marker or therapeutic target for oesophageal cancer.

**Keywords:** Oesophageal cancer, Esophageal Neoplasms, Systems Biology, STRING, Cytoscape

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**P1.4**

**Protein Protein Interaction Network and Enrichment Analysis of Genes in Bone Cancer**

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**Background:** Bone cancer can start in any bone in the body, but it most often impacts the pelvis or the long bones in the arms and legs. Bone cancer is uncommon, making up all things considered to be less than one percent. There are three types of bone cancer which is Chondrosarcoma, Ewing sarcoma, and Osteosarcoma. Many signs of bone cancer are noted, such as bone pain, inflammation and tenderness close the impacted region, weakening the bone, causing an easy fracture, easy tiredness, and unexpected weight loss. The aim of this research is to analyze the network of bone cancer's protein-protein interaction and recognize important genes engaged in bone cancer. **Methods:** A total of 116 genes have been obtained from the uniport database causing bone cancer. The protein-protein interaction network was constructed and analyzed using STRING and Cytoscape 3.7.1 tools. In addition, a functional enrichment analysis was performed to identify key genes using the CentiScape and FUNRICH databases. **Results:** Based on network topological parameter, BRCA2, EIF4A3, GNB2L1, PPP2R5A and PARK2 were identified as the key gene in the network. Among them, the PARK2 gene was obtained as a hub gene with the highest Betweenness Centrality (BC) and node degree. The functional enrichment analysis was done using FUNRICH database. **Conclusion:** The network analysis will help in prioritizing genes in the pathway that helps in understanding the underlying mechanism of disease. From this study, Parkin RBR E3 ubiquitin protein ligase (PARK2) was identified as a key gene involved in bone cancer. Thus, further study on this gene and their biological mechanism and pathway may, therefore, provide a potential target for the treatment of bone cancer.

**Keywords:** Bone cancer, Sarcoma, Ewing, protein-protein interaction network, Cytoscape

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**P1.5**

**Systems Biology Approach to Identify Key Genes Involved in Laryngeal Cancer**

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**Background:** Globally, laryngeal cancer (LC) was the most common type of cancer in men. The most frequent occurrence in the region of head and neck. LC has a high mortality rate depending on the diagnosis of the disease at an early stage. Of these cancers, more than 90% were squamous cell carcinomas (SCC) among LC. However, the pathogenesis of LC and its associated biological procedures and pathways is poorly understood. Protein-protein interaction (PPI) network analysis can provide an informative idea and detail scheme for an understanding of the molecular or biological mechanisms of laryngeal cancer pathogenesis. In this study, a system biology method was used based on accessible proteomics literature information as a rational strategy to disclose novel particular markers and likely laryngeal cancer therapeutic objectives. **Methods:** The PPI Network was constructed and analyzed using laryngeal Cancer genes obtained from the NCBI database based on literature studies and the network was analyzed using STRING 10.0 and Cytoscape 3.7.1 software. Using Funrich v 3.1.3 software, functional enrichment of identified genes was also performed. **Results:** The identified key genes were NCOA3, CREBBP, ESR1, POLR2A, BRCA1 based on network topology analysis. Among them, the BRCA1 gene was obtained as the highest betweenness centrality and node degree. In addition, the
cellular component, molecular function, biological process, and a biological pathway was analyzed using functional enrichment analysis tools. **Conclusion:** From previous studies it is identified both BRCA1 and BRCA2 mutations involved in various cancer. In this study, through the network analysis we identified BRCA1 as key gene involved in laryngeal Cancer. Thus, a detailed study on the biological mechanism of this gene and pathways may provide a potential target for the treatment of Laryngeal cancer.

**Keywords:** Laryngeal cancer, Laryngeal Neoplasms, Protein Interaction, Systems biology, Cytoscape

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### P1.6

**A Study on the Potential Role of Sox2, An Embryonic Stem Cell Transcriptional Factor, in the Tumourigenicity of Pancreatic Ductal Adenocarcinoma**

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**Background:** Cancer stem cells (CSCs) are highly tumourigenic subset of cells within a solid tumour of pancreatic ductal adenocarcinoma (PDAC), which are the culprit of tumourigenesis. These CSCs maintain their tumourigenic potential, while giving rise to their non-tumourigenic progenies through self-renewal. Here, we investigated the tumourigenicity of PDAC cell lines in vitro and in vivo as readouts of the existence of CSCs, which are supposed to be SOX2-expressing cells. **Methods:** Tumorsphere assay, a hallmark evaluation of self-renewal potential in vitro was performed on PDAC cell lines: BxPC-3, PANC-1, Capan-2, and MIA PaCa-2. A formation of multicellular sphere-like colonies indicates an enrichment of CSC subpopulation. Sox2 expression in Capan-2 tumourspheres was analysed by Western blotting. To assess in vivo tumourigenicity of PDAC cell lines, a group of six immunocompromised mice was inoculated with 10⁵ and 10⁶ cells of each cell line. SOX2-expressing cells within the tumour xenograft were detected by immunohistochemical (IHC) staining. **Results:** In serum-free and non-adherent culture conditions, a small proportion of BxPC-3 and Capan-2 cells clonally expanded into tumourspheres. SOX2 expression was found to be up-regulated in Capan-2 tumourspheres as compared with its monolayer culture. Kaplan-Meier analyses suggested that BxPC-3 and Capan-2 cells are equally tumourigenic, while PANC-1 and MIA PaCa-2 cells are relatively less tumourigenic. IHC staining revealed that SOX2-expressing cells were present in BxPC-3, Capan-2, and PANC-1 tumour xenografts. **Conclusion:** Previous studies showed that stem cell-like characteristics of PDAC cells are attributed to SOX2 expression in vitro. Our present study provides an insight into the role of SOX2 in the tumourigenesis of PDAC in a tumour xenograft model. Our findings revealed that the presence of putative CSCs, which are highly tumourigenic in vivo, can be predicted by an existence of tumoursphere-forming cells within a PDAC cell line. However, these CSCs are not correlated with SOX2-expressing cells.

**Keywords:** Cancer stem cells; Pancreatic ductal adenocarcinoma; Tumourigenicity; Tumourspheres; SOX2

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PL8
Comparative study of anti-cancer drugs induced myelotoxicity and lung metastasis with ionizing radiation in mice model

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Background: The magnitude of toxicity or severe side effects induced by drugs or radiation is not well tolerated by many patients and could develop problematic conditions such as secondary cancer, cancer recurrence and degenerative diseases. This study was conducted to compare the severity of anti-cancer drugs induced myelotoxicity and metastatic cancer with ionizing radiation in a Balb mice model.

Methods: Myelotoxicity was induced by a single injection of 5-fluorouracil (125mg/kg) or Cisplatin (40 mg/kg), administered to 7-week-old Balb/c mice on day 0, 1, 3, 5, 7, 9 and 11. Another group of mice were exposed to a gamma-radiation dose of 6 Gy on day 0, 1, 3, 5, 7, 9 and 11 before tumour inoculation. The mice were inoculated with B16F10 cells (3×10⁵/200 uL) via tail vein injection for anti-cancer and radiation induced group mice or with D-PBS as a non-irradiated group at the same day. The mice were sacrificed by cervical dislocation on each of days and lung tissue was examined after H and E staining for histopathology. In a double blind setting, the total number of lung metastasis tumour was examined by macroscopic inspection.

Results: Varied results showed and the severity of leukopenia was high significantly in 5-fluorouracil treated mice than Cisplatin. The number of lung metastatic tumours was remaining high in both groups. The irradiated groups showed initial increase in the number of metastatic tumours but at the end of 11 days period significantly reduced.

Conclusion: The present study concluded that anti-cancer drugs as well as the limited and controlled radiation-induced myelotoxicity did not help to develop metastatic tumours further.

Keywords: Cisplatin, Myelotoxicity, 5-fluorouracil, Gamma radiation, leukopenia, anti-cancer drugs

PL10
Effect of DNA Methylation of CPG Island on Choline Kinase Alpha Promoter Activity

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Background: Choline kinase (CK) enzyme is involved in the biosynthesis of phosphatidylcholine, the major constituents of cell membranes. One of its isoform, CK alpha, has been implicated in carcinogenesis. CpG islands, targets of DNA methylation are often associated with activities of gene promoters and play important roles in gene regulation. Thus, this study aims to investigate the effect of DNA methylation on the promoter activity of chka gene promoter in breast cancer cell line.

Methods: Four CpG islands on the chka promoter region were identified using MethPrimer software. A 2000 bp wild type chka promoter and CpG island deletion mutants were cloned into pGL4.10 vector, treated with methyltransferase (M.SssI) before transient transfection into MCF-7 cells and assayed for promoter activity.

Results: Deletion of a specific CpG island located between -227 to -53 bp upstream of the ATG translation start site significantly increased (~2.5 fold) the promoter activity compared to the full length promoter. The promoter activity of methylated full length promoter sequence was also significantly lower than the methylated deletion mutant (~6 fold) and unmethylated full length (~8.5 fold) promoters. The results suggest that this particular CpG island contains elements for the binding of suppressor transcription factor and the binding could be regulated by DNA methylation.

Conclusion: The study provides a perspective on the involvement of CpG island and DNA methylation in the transcriptional control of chka gene.

Keywords: choline kinase, carcinogenesis, promoter, CpG island, DNA methylation
**PI.12**

**Determination of Optimal Dose for N-ethyl-N-nitrosourea-Induced Leukaemia-Lymphoma in Rats**

Nurul Syahirah Ahmad Sayuti¹, Rosly Shaari Mohd², Noordin Mohamed Mustapha¹, Mazlina Mazlan¹, Azrina Azlan¹, Farhan Hanif Mohd Reduan¹, Aliyu Abdullahi¹, and Hazilawati Hamzah¹*¹

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**Background:** Chemically induced cancer had been most common used in the animal model to mimic the clinical cancer progress. **Method:** This study aims to determine the appropriate dose of N-ethyl-N-nitrosourea (ENU) that could be used to induce leukaemia-lymphoma in male Sprague Dawley rats. A total of 32 male rats were divided equally into four groups namely groups A (control), B (60mg/kg ENU), C (65 mg/kg ENU) and D (70 mg/kg ENU). The ENU was administrated intraperitoneally (i.p) to rats in groups B, C and D at the respective dose of 60, 65 and 70 mg/kg body weight per injection for 4 injections in a 2-week period at the beginning of the experiment. The rats were observed daily for 24 weeks for their mortality rate, behavioural and physical changes. At the end of the experiment, all rats were humanely sacrificed and blood samples were collected. Blood and serum samples were examined for the presence of leukaemic cells and changes in the serum biochemical parameters using standard methods. **Results:** Rats in group B survived throughout the experimental period. Mortality rates of 25% (2 of 8 rats) and 37.5% (3 of 8 rats) in groups C and D at the 20th and 8th weeks of the experimental period, respectively. Meanwhile, regardless of the concentration of ENU exposed to the rats, blastic cells were detected on blood smears of all rats that were exposed to the carcinogen, anaemia was not detected in all ENU-exposed groups, but significant elevations in serum alkaline phosphatase (ALP), creatine kinase (CK) and lactate dehydrogenase (LDH) were recorded. **Conclusion:** In conclusion, based on this study, the appropriate dose to induce leukaemia-lymphoma in rats is at low dose, which is 60 mg/kg of body weight.

**Keywords:** Serum biochemistry, blastic cells, chemical carcinogen

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**PI.13**

**Down-regulation of Purine Nucleoside Phosphorilase (PNP) Affect Protein Salvage Pathways in Ovarian Cancer Cell Line A2780 Treated with 9-methoxycanthin-6-one**

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**Background:** Ovarian cancer ranked among the top of the deadliest cancers of female reproductive system. At present, standard treatment for ovarian cancer involves chemotherapy drugs paclitaxel and carboplatin after surgical to remove tumor to prolong patients’ life. However, the use of these drugs often leads to drug resistance that cause potential death of patients. The needs of new therapeutic agent lead to many cancer research worldwide. Our research discovers that plant compound 9-methoxycanthin-6-one derived from Malaysia local plant Eurycoma longifolia has active *in vitro* anti-cancer effects against ovarian cancer cell line A2780. Proteomics study was conducted with the aim to elucidate the modes of action of 9-methoxycanthin-6-one via identifying key proteins being affected in causing cancer cell death on A2780. 9-methoxycanthin-6-one down-regulated one of the key proteins; Purine Nucleoside Phosphorilase (PNP) in ovarian cancer cell lines. **Methods:** Initially, protein extracts preparation for ovarian cancer cell line-A2780 untreated and treated with 9-methoxycanthin-6-one was performed using lysis buffer. The proteins were separated using 2D-gel electrophoresis and differential analysis were performed on the protein expressions and suppression between these two samples. Proteins identification were performed by matching the peptide sequence resulted from tryptic digestions that was analysed by MALDI-TOF/TOF mass spectrometer with Mascot database. Ingenuity Pathway Analysis (IPA) was
then used to analyze protein networks affected due to 9-methoxycanthin-6-one treatment. Results: 9-methoxycanthin-6-one caused down-regulation of protein PNP in ovarian cancer cell line-A2780. PNP is a ubiquitous enzyme of purine metabolism and also an oncogene protein. Ingenuity Pathway Analysis shows that down-regulation of PNP may lead to suppression of Protein Salvage pathways such as Xanthine and Xanthosine Salvage, Guanine and Guanosine Salvage and Adenine and Adenosine Salvage. In normal cell condition, PNP enable cells to synthesize purine nucleotides from purine bases activity for cell survival and function. Thus, the down-regulation of PNP in this study may suggest an interference of cell survival which leads to inhibition in growth of ovarian cancer cells when treated with 9-methoxycanthin-6-one. Conclusion: Down-regulation of protein PNP cause suppression of protein salvage pathways where protein synthesis failed to function. Future work on protein validation via western blotting can be done to confirm the key protein.

Keywords: Protein Salvage pathways, Ingenuity pathway analysis, Eurycoma longifolia, A2780, oncogene

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P2.1 Synthesis and SAR Studies of New Chromone Derivatives as Inhibitors of PGE2 Production

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Background: Prostaglandin E2 (PGE2) is an essential metabolite of the cyclooxygenase pathway in the human body. However, excessive production of PGE2 has been implicated with a variety of inflammatory and cancer diseases. Studies have revealed that blockade of PGE2 production could enhance the innate immune function both in vitro and ex vivo experiments. Hence, this could serve as a useful strategy for preventing and treating inflammation and cancer in related individuals. Natural products have been of great interest for many years, and have provided modern medicine with numerous useful drug leads. One of the families of natural products that has been widely explored for their biological activities is the chromones. Methods: A series of chromone derivatives were chemically synthesised, purified with column chromatography and characterised by NMR and HRMS. The compounds were then screened for their effects on PGE2 secretion levels in the U937 cells and human recombinant COX-2 enzyme. Apart from that, the effects of the selected compounds on PGE2 production were also evaluated using the human whole blood assay. Results: The most potent compound 2 exhibited a dose-response inhibition on PGE2 production in LPS/IFN-γ stimulated in U937 cells with an IC50 value of 8.5 μM. The cells remained viable at the IC50; thus, the inhibitory effect upon PGE2 secretion was not due to cell death. Compound 2 displayed an IC50 value of 2.7 μM when tested in the LPS-stimulated human whole blood assay. Compound 2 merely inhibited 37% of the activity of the purified human recombinant COX-2 enzyme at a concentration of 20 μM. Conclusion: It can be concluded that compound 2 could possibly block the PGE2 production both in LPS/IFN-γ stimulated in U937 cells and human whole blood assay by targeting the upstream signalling proteins that regulate the activity of COX-2. This important piece of information obtained from the study will be utilised in the next design of more potent anti-inflammatory agents.

Keywords: Chromone, prostaglandin E2, structure-activity relationship and inflammation

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P2.2
Assessment of Cytotoxic Activity of Selected Semi-Synthetic Andrographolide Analogous in Breast and Colon Cancers Cell Lines

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Background: Cancer is a major life-threatening illness that leads to serious problems worldwide. Most common types of cancer are breast, lung, colorectal and liver. Andrographis paniculata (Burm. F.) Wall. Ex. Nees (Chuan Xin Lian) is a well-known traditionally used medicinal herb which contains two major bioactive secondary plant metabolites which are andrographolide (AGP) and 14-deoxy-11, 12-didehydroandrographolide (DDAG). The aim of this study is to identify potent and selective compounds that displayed cytotoxicity against MCF-7 breast and HCT-116 colon cancers cell lines. Methods: To determine the cytotoxic effect of the tested compounds, using methylthiazol tetrazolium (MTT) assay. The half-maximal inhibitory concentration (IC₅₀), growth inhibition concentration (GI₅₀), total growth inhibition (TGI) and lethal concentration (LC₅₀) were obtained via semi-log dose-response curves. Results: Overall, the AGP derivatives showed improved cytotoxicity than parent compound against HCT-116 cell line with SRS 50 > SRS 07 > SRS 58 > SRS 21 > AGP>DDAG based on the IC₅₀ values. None of the AGP derivatives showed improved cytotoxicity than parent compound against MCF-7 except SRJ 58 which SRS 50 > AGP > SRS 21 > SRS 07 > SRJ 58 > DDAG based on the IC₅₀ values. Conclusion: All AGP and AGP derivatives showed more selective cytotoxic activity against HCT-116 cell line. DDAG showed the least cytotoxic activity against both HCT-116 and MCF-7 cell lines.

Keywords: Andrographis paniculata, Andrographolide, MTT, MCF-7, HCT-116

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P2.3
Improving the Delivery of Antimetastatic Compound Stattic by Self-Assembled Amphiphilic Pendant-Dendron Copolymers in Breast Cancer Cell Lines

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Background Stattic is a known inhibitor of STAT3 signalling mechanism, which is involved in the development of tumour metastasis. However, the clinical application is limited by its hydrophobicity and high effective dose. It is believe that such limitations could overcome by encapsulating Stattic with an amphiphilic pendant-dendron copolymeric nanocarrier, P₇₁D₃ micelles to deliver the drug to the target tumour. Methods: P₇₁D₃/Stattic micelles were prepared by rotary evaporation method. Physicochemical characterisation of the P₇₁D₃/Stattic was determined by using dynamic light scattering, uv-vis spectrophotometry and transmission electron microscopy. The release profiles of Stattic from P₇₁D₃/Stattic micelles in different solutions were determined by a dialysis method. P₇₁D₃/Stattic micelles were also assessed for their in vitro cellular toxicity (MTT assay) and antimitogization (wound healing and transwell assays) efficacy on human and murine breast cancer cell lines. Results The P₇₁D₃ copolymers self-assembled into micelles, encapsulating Stattic, to form spherical P₇₁D₃/Stattic micelles with 100 – 200 nm diameter and a drug loading ranging from 10 – 100 %. P₇₁D₃/Stattic micelles gave higher drug release (32%) under tumouric acidic condition (pH5.3) compared to a physiological neutral condition (14%). Unexpectedly, a rapid and high drug release was observed in a simulated plasma solution. P₇₁D₃/Stattic micelles were found to give significantly higher cellular toxicity (30 - 90 folds more potent),
as well as improved antimigration efficacy (3 - 6 folds decrease in inhibitory concentration) compared to free Stattic in MDA-MB-231 and 4T1 cells. Conclusion P71D3 micelles served as a good solubilising agent for Stattic, allowing the encapsulation of Stattic in the P71D3 micelles. The P71D3/Stattic micelles effectively enhanced the potency of the drug as determined from the in vitro studies. The cellular toxicity and anti-migration properties suggested that the P71D3/Stattic micelles could be a promising antimetastatic agent, which is worth for further studies.

Keywords: Drug delivery, nanocarrier, diblock copolymer micelles, anti-metastasis, Stattic.

P2.6
Prescreening of Crude Extract of Actinomycetes from East Malaysia Soil for its Antitumor Properties

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Background: Extensive research has been done especially in mining new antitumor drugs. Actinomycetes are classified as gram-positive bacteria which are known to produce vast amount of useful secondary metabolites has grasped worldwide attention due to its useful secondary metabolites. East Malaysia namely as Sabah and Sarawak is rich with their diversity of microorganism from soil. The aim of this study is to screen and investigate the antitumor property of actinomycetes obtained from soil in East Malaysia against two different cancer cell lines. Method: All of the actinomycetes isolated were screened against two cancer cell lines, which are HeLa and HepG2 due to the abundance cases of cervical cancer and liver cancer in East Malaysia. Results: Two of the selected actinomycetes isolates showed significant antitumor activity with IC50 value of 10.52±0.88 µg/ml and 22.45 ± 0.92 µg/ml. Conclusion: Further investigation is needed to investigate the 16s rRNA sequences of these isolates and to obtain information on phylogenetic tree which will enables us to understand the evolution of these Actinomycetes from East Malaysia.

Keywords: Actinomycetes, antitumor, cell line

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P2.7
FICUS DELTOIDEA Mucoadhesive Dual Antimicrobial Loaded Gel for the Treatment of Periodontal Disease

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Background: Ficus deltoidea is a common medicinal plant traditionally used in Southeast Asia countries including Malaysia. Previous studies demonstrated that Ficus deltoidea has a wide variety of medical importance including antibacterial, antithrombotic and anticancer. The purpose of this study is to formulate Ficus deltoidea mucoadhesive dual antimicrobial loaded gel for the treatment of periodontal disease. Methods: Ficus deltoidea leaves extract was isolated by decoction method and formulated as dental mucoadhesive gel by varying concentration of two different mucoadhesive polymers (sodium carboxymethyl cellulose and hydroxypropyl methylcellulose). Evaluations were performed on the Ficus deltoidea leaves extract and the mucoadhesive gel. Antibacterial activity was evaluated by agar diffusion method. Results: The yield of Ficus deltoidea leaves extract obtained was 23% w/w. Swelling index of the mucoadhesive gel was within 16.30±1.76% (F4) to 29.62±1.73% (F3) and mucoadhesive force was 6.59±0.33 g (F1) to 11.51±0.83 g (F3) over 30 days. The swelling index and mucoadhesive force were shown to be influenced by types and concentration of polymers used. Positive results obtained in antibacterial activity have exhibited zone of inhibition 14.00±2.65 mm (F6) to 29.67±1.53 mm (F1). The zone of inhibition was suggested to be affected by extract concentration as well as types and concentration of polymers. Conclusion: In conclusion, sodium carboxymethyl cellulose oral gel was thermoresponsive, mucoadhesive, syringeable, and released drugs in slow and controlled manner with effectiveness against broad range of microbes. Future anti-cancer research activities on chemopreventive effects of Ficus deltoidea on OSCC cells using rat animal model will be conducted.
**Keywords:** Ficus deltoidea leaves extract, dental mucoadhesive gel, swelling index, mucoadhesive force, antibacterial activity

**P2.9**

**Anti-Proliferative Effects of Aquilaria malaccensis Extracts Against A2780 Ovarian Cancer Cells**

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**Background:** Aquilaria malaccensis or karas is regarded as an important local medicine to relieve mild and chronic inflammation. Despite their wide ethno-pharmacological use among Asians, its anti-proliferative effects have not been thoroughly investigated except on the bark and leaves. As such, the present study assessed the potential anti-proliferative activities of the fruits of A. malaccensis. **Methods:** The fresh fruits of A. malaccensis were extracted using aqueous, methanol, ethanol, chloroform and hexane. Each extract was screened against ovarian cancer cells (A2780) and normal liver cells (WRL-68) for 72 hours. Sulforhodamine B assay was used to analyse the percentage of cell density and half maximal inhibitory concentration (IC50) of the treated cells. **Results:** All fruit extracts of A. malaccensis exhibited strong anti-proliferative activities against ovarian cancer cells and normal liver cells with rank of potency from very active, active to moderately active. The IC50 value of chloroform extract against ovarian cancer cells was less than 1 µg/mL (very active), while the ethanolic extract gave IC50 of 6.12 ± 0.05 µg/mL (active). Hexane, aqueous and methanolic fruit extracts, on the other hand, showed moderate activities with IC50 values of 23.72 ± 0.89 µg/mL, 26.51 ± 0.46 µg/mL and 28.60 ± 0.57 µg/mL, respectively. As for normal liver cells, the fruit extracts of A. malaccensis inhibited the proliferation of cells in a similar manner as ovarian cancer cells with IC50 values of <1 µg/mL (chloroform), 6.05 ± 0.11 µg/mL (ethanol), 21.24 ± 1.04 µg/mL (hexane), 28.98 ± 0.40 µg/mL (aqueous) and 32.86 ± 0.76 µg/mL (methanol). **Conclusion:** These anti-proliferative results demonstrated that A. malaccensis may potentially serve as a new option for drug discovery and development. This warrants isolation and characterization for the active compound(s).

**Keywords:** Aquilaria malaccensis, karas, A2780, ovarian cancer cells, in vitro, methanol, ethanol, chloroform, hexane, aqueous

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**P2.10**

**Potential Anti-Metastatic Property of Novel Andrographolide and 14-Deoxy-11,12-Didehydroandrographolide Analogues in Melanoma**

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**BACKGROUND:** Andrographolide (AGP) and 14-deoxy-11,12-didehydroandrographolide (DDAG) are major natural terpenes found in Andrographis Paniculata. Both compounds were reported to possess different therapeutic activities against various diseases such as cancer. As these compounds bear these great potentials to be developed as drugs, both of them had been semi-synthesized to improve biological activities. Many of these semi-synthesized AGP and DDAG analogues were found to have improvement in anti-proliferation activity against different cancer cells. However there were no studies conducted to investigate anti-metastatic activity in AGP and DDAG analogues. We hypothesized that these analogues could possibly possess anti-metastatic activity. In this study, novel analogues of AGP and DDAG (SRS27, SRS49, SRJ09 and SRJ23) were selected to study the potential anti-metastatic property on B16-F10 cell line. **METHODS:** Our approach is to determine the half maximal growth inhibitory concentration (IC50) and highest non-cytotoxic dose (IC90) of these analogues in B16-F10 cells by using...
MTT assay. To test the potential anti-metastatic activity of these compounds, we utilize scratch assay to measure the percentage of migratory cells treated with IC_{50} and IC_{80} of these analogues in scratched area after. **RESULTS:** Despite of the compounds especially Andrographolide analogues (SRJ09 and SRJ23) possessed potent inhibition on B16-F10 cell proliferation, we observed that none of the analogues were capable of inhibiting B16-F10 cell migration effect. **CONCLUSION:** Andrographolide and 14-deoxy-11,12-didehydroandrographolide analogues have anti-proliferation effect but not anti-migration effect. Further studies such as matrix metalloproteinase (MMP) expression and different cell migratory assay (matric gel invasion assay) need to be conducted to confirm our hypothesis.  

**Keywords:** melanoma, metastasis, B16-F10, andrographolide, 14-deoxy-11,12-didehydroandrographolide

### P2.11

**Chemical Profiling and In-Vitro Anti Proliferative Activities of Eurycoma Longifolia Leaves Extracts**

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**Background:** *Eurycoma longifolia* Jack or Tongkat Ali is one of the species from Simaroubaceae family that has gained notoriety for its medicinal properties such as treating dysentery, glandular swelling, persistent fever and malaria. This plant is reported to contain several classes of chemical compounds such as quassinoids, alkaloids, squalene derivatives, triterpenes and biphenylneolignans related to anti-cancer activity. In the present study, we aimed to establish a chemical profile from ethanolic extract of *E. longifolia* leaves via High Performance Liquid Chromatography (HPLC), along with an evaluation of anti-cancer activities. **Methods:** Dried leaves of *E. longifolia* were extracted using ethanol. Ethanolic extract analysis was performed using reverse phase HPLC in a gradient phase consisting of 0.1% trifluoro acetic acid and acetonitrile, whereas its anticancer properties were evaluated against ovarian (A2780), colorectal (HT-29) and breast (SKOV-3) cancer cell lines as well as normal liver (WRL-68) cell line in vitro. **Results:** The HPLC profiles showed a major bioactive compound at a retention time of 7.8 minutes and has yet been identified. IC_{50} values for ovarian A2780, colorectal HT-29 and breast MCF-7 cancer cell lines were 12.46 μg/mL, 54.54 μg/mL and 73.01 μg/mL respectively, while normal liver WRL-68 cell line was 218.67 μg/mL. **Conclusion:** Ethanol extract of the leaves of *E. longifolia* showed a selective anti-proliferative effect on ovarian cancer cell line but not on normal liver cell line. The unknown compound that appears to be the major derivative may contribute to the anti-cancer activities.  

**Keywords:** *Eurycoma longifolia*, Tongkat Ali, anti-cancer, HPLC, SKOV-3, HT-29, A2780  
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### P2.12

**Synthesis and Cytotoxic Evaluation of Monoketone and Diketone Asymmetric Curcumin Derivatives as New Anti-Breast Cancer Agents**

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**Background:** Breast cancer is one of the leading causes of death among women. Thus, finding new and potent anticancer agents remains an urgent need. In this study, we designed and synthesised 30 asymmetric curcumin derivatives, which can be classified into two main series: monoketone and diketone derivatives. **Methods:** All compounds were evaluated for their cytotoxicity activity against the hormone-dependent (MCF-7) and triple-negative breast cancer (MDA-MB-231 and HCC 1806 cell lines) at 10 μM with MTT assay. **Results:** Our results showed that 9 monoketone compounds were effective in reducing the cells viability in MCF-7 and MDA-MB 231 cell lines to ≤ 10%. Among them,
compound bearing with nitro moiety (4) displayed the most potent inhibitory activity on MCF-7 and MDA-MB-231 (IC₅₀ values were 0.38 µM and 0.39 µM, respectively). In contrast, 10 diketone compounds exhibited either weak or inactive inhibitory activities against all the cell lines except for a compound bearing trifluoro moiety (25), which successfully inhibited MCF-7 (IC₅₀ values was 2.3 µM). However, all compounds were least active against HCC-1806. **Conclusion:** Collectively, these results guide us further for the selection of lead compound(s) towards comprehensive anticancer activity evaluation.

**Keywords:** Asymmetric curcumin, Monoketone, Diketone, Synthesis, Anticancer

### P2.13 In vitro Cytotoxic and Antioxidant Potentials of Methanolic Extracts of Tectona grandis Leaves

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**Background:** Tectona grandis (Verbenaceae) or locally known as teak, is well known for its durable wood which has great commercial value given its dimensional stability and hardness that resists decay process without protection with paints and preservatives. Owing to its astringent and diuretic properties, T. grandis is also traditionally used for treatment against swelling, bronchitis, biliousness, hyperacidity, diabetes and leprosy. Extracts prepared particularly from its leaves have been widely used in the folklore for treatment against various kinds of wounds, especially burn wounds. The extracts were also used as anti-inflammatory agent for topical application on burns. Although there are several reports on the cytotoxicity of T. grandis bark and wood, such activity has yet to be reported for T. grandis leaves.

**Methods:** Methanolic extracts of T. grandis leaves, twig and bark were evaluated for their respective cytotoxic activity against ovarian (SKOV-3), colorectal (HT-29) and breast cancer (MCF-7) cell lines. The extracts were also evaluated for their antioxidant potential using DPPH assay. The cytotoxic activities (IC₅₀ values) of the extracts were evaluated using sulforhodamine B and MTT assays.

**Results:** The methanolic extract of T. grandis leaves showed cytotoxic potential against the selected cancer cell lines with IC₅₀ values < 10 µg/mL. While extracts from twig and bark showed less cytotoxic potential with IC₅₀ values > 80 µg/mL. All extracts also demonstrated antioxidant potential by showing high percentage of inhibition against DPPH radical scavenging activity. **Conclusion:** The methanolic extract of T. grandis leaves showed potential cytotoxicity and antioxidant activity against selected cancer cell lines. More in-depth studies will be carried out to investigate the chemical constituents in the leaves that are responsible for the observed activities.

**Keywords:** Tectona grandis, teak, cytotoxic, antioxidant

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### P2.14 Target Identification of Saccharides-Induced Apoptosis in Caco-2 Cells by Structure Similarity Search and Molecular Docking

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**Background** Keratinocyte growth factor (FGF7) mediates its effect through binding specifically to its receptor (FGFR) and promote receptor dimerization, this activates receptor intercellular tyrosine kinase domain followed by auto-phosphorylation to allow specific intracellular molecules to propagate the signal from the cell surface. Activation of FGFR regulates differentiation, proliferation and migration of cancer cells. Elevated levels of FGF7 are detectable in patients with colorectal cancer. FGF7 is currently
the potential target to develop anticancer drugs through inhibiting the deregulated blood vessel formation in cancer cells. Practically it would be impossible to test each drug-like compound for every possible molecular target. For that reason, computational methods such as structure similarity search and molecular docking can be used to fill this gap and identify the possible targets for each individual molecule. **Methods** In this study we investigated the cytotoxic effect of different saccharide molecules [β-cyclodextrin (β-CD) and β-lactose (β-Lac)] using real-time xCELLigence technology on Caco-2 cell line. To identify their molecular targets, structure similarity search was performed using Swiss Target Prediction software followed by molecular docking towards FGF7 using MOE.2014 software. **Results** Target prediction and molecular docking results revealed that both molecules have potential to target FGF7. In case of β-Lac, it was based on 3D similarity to CHEMBL2303729 with score of 0.804 and for β-CD CHEMBL198643 with score of 0.959. Molecular docking results have demonstrated that β-CD has the highest affinity toward FGF7 with docking score of -5.931 (RMSD = 1.543) and β-Lac with docking score of -4.457 (RMSD = 2.689). Assessing their cytotoxic effect in the presence of exogenous FGF7, both β-CD and β-Lac were cytotoxic to Caco-2 cells with IC50 of 5.22 μM and 5.31 μM, respectively. **Conclusion** These findings suggested the need for developing novel, carbohydrate-based therapeutic as anticancer agents.

**Keywords:** Saccharides, FGF7, computational methods, cytotoxicity, real-time xCELLigence technology

**P2.15**

**In-silico Docking Simulations of Molecular Interaction between Betulnic Acid and Bcl-2 Anti-Apoptotic Proteins**

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**Background:** Betulinic acid, a pentacyclic lupane-type triterpene, has been reported as a potential anticancer agent that induces apoptosis in many cancer types. B cell lymphoma-2 (Bcl-2) protein is an anti-apoptotic member of the Bcl-2 family, key regulators of programmed cell death or apoptosis. Overexpression of anti-apoptotic Bcl-2 proteins is associated with the inhibition of cell cycle progression. The present study investigated the interactions of betulinic acid with Bcl-2 proteins using molecular docking simulations. **Methods:** AutoDock Vina was applied to investigate the binding affinity and the binding modes of betulinic acid on Bcl-xL (PDB ID: 2LPC), Bcl-W (PDB ID: 1MK3) and Mcl-1 (PDB ID: 2MHS) proteins. The three-dimensional (3D) structures of Bcl-2 proteins were taken from the Protein Data Bank (PDB). The best binding mode were analyzed using protein-ligand interaction profiler (PLIP) server. **Results:** The docking results revealed that betulinic acid showed good binding affinity against Bcl-xL, Bcl-W and Mcl-1. The most hydrophobic interactions were observed in Bcl-W which had formed one interaction with Ala64 and Ala74, and two interactions with Leu105. The hydrogen bonds were predominantly found in Bcl-xL receptor; one hydrogen bond exists with Trp24 at distances 3.03 Å and two hydrogen bonds with Ser25 at distances 3.07 Å and 2.81 Å, respectively. **Conclusion:** The obtained results warrants further implemented for development of chemotherapeutic agents based on betulinic acid.

**Keywords:** betulinic acid, Anti-apoptotic, Bcl-2, molecular docking

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**P2.16**

**In vitro Studies of Synsepalum Dulcificum Fruits: Antimicrobial and Anticancer Activities**

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**Background:** Synsepalum dulcificum plant belongs to the family of sapotaceae which well known as miracle fruit. Red berries of Synsepalum dulcificum, which is an evergreen shrub native of tropical West Africa, have a unusual property in modifying taste buds of the tongue that makes every sour or acidic food eaten or drunk to taste very sweet. **Methods:** The phytochemical composition of the plant is determined by systemic phytochemical screening method, MIC breakpoint, antimicrobial activity of three different extracts of Synsepalum dulcificum fruit is performed by agar well diffusion method against six bacterial strains Bacillus subtilis, Staphylococcus aureus, Streptococcus pyogene, Pseudomonas aeruginosa, Klebsiella Pneumoniae and Proteus vulgaris and anticancer activity of ethanol extract on two different colorectal cancer cell lines HCT-116 and primary colon epithelial (PCE) cell line is performed by MTT assay. Different concentration (5, 10 and 20 mg/mL) of plant extracts (petroleum ether and ethanol) were tested against each type of bacterial strain. Different concentrations ranging from 7.8 μg/mL to 1000 μg/mL were tested against each cell lines. **Results:** The phytochemical analysis revealed the presence of alkaloid, phenolic, carbohydrate, tannin, glycoside and saponin. The presence of these compounds might be responsible for the antimicrobial and anticancer activities. Extracts of Synsepalum dulcificum fruits showed broad spectrum of antimicrobial activity when compared to standard antibiotic, Tetracycline (0.05 mg/mL). Both petroleum ether and ethanol extracts of Synsepalum dulcificum fruits has demonstrated antimicrobial activities against all bacterial strains. Ethanol extract of Synsepalum dulcificum fruits showed cytotoxic activity when compared to standard control, Fluorouracil (10 μg/mL). EESD against HCT-116 is highly toxic due to the concentration value of less than 20 μg/mL when it is at 50% of cell viability. **Conclusion:** Synsepalum dulcificum fruits has high potential for treatment of colorectal cancers.

**Keywords:** Synsepalum dulcificum, phytochemical activity, minimum inhibitory concentration, antimicrobial activity, anticancer activity

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**P2.18**

**Triamcinolone Acetonide Tablets for Buccal Delivery**

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**Background:** Buccal drug delivery system allows drugs to be delivered within or through buccal mucosa. The aim of this study was to formulate and characterise triamcinolone acetonide buccal bilayer tablets. Acetonide salt of triamcinolone is a synthetic glucocorticosteroid with immunosuppressive and anti-inflammatory activities. Previous studies demonstrated that triamcinolone acetonide could be used to treat oral lichen planus whereby there are areas of white lines with a reddish border, possibly with ulceration. Many oral lesions may be precancerous. Cancer may develop if the lesions are left untreated. Triamcinolone acetonide might be the drug of choice to prevent oral lichen planus from becoming cancerous. **Methods:** The tablets were formulated by direct compression using polymers poloxamer 407, HPMC, SCMC, PVA and EC with other excipients. The prepared tablets were evaluated for their physicochemical parameters. **Results:** FTIR indicated no interaction between the drug and polymer. All results were within the Pharmacopeial limits. Tablets containing Polaxamer 407 showed good swelling properties, mucoadhesive time (465 minutes) in the goat’s buccal mucosa and sustained in vitro drug release (more than 6.5 hrs). Data of in vitro drug release which were fed into several kinetic models showed first order and non-Fickian diffusion. **Conclusion:** The triamcinolone acetonide tablets were developed as an alternative to conventional dosage forms with an added advantage of circumventing the hepatic first pass metabolism. This warrants further studies of the potential use of triamcinolone acetonide for prevention of precancerous oral lichen planus.

**Keywords:** Triamcinolone acetonide, buccal tablet

**P2.19**

**Molecular mechanism underlying anticancer effect of tricyclohexylphosphinegold (I) mercaptobenzoate against MCF-7R and A2780 cells**
Background: Metal complexes including gold complexes possess various medical therapeutic benefits. A series of gold complexes was synthesized from the precursor tricyclohexylphosphinegold(I) and mercaptobenzonic acid ligands. The Tricyclohexylphosphinegold(I) R-mercaptopbenzoate derivatives were yielded at different ligand position of ortho (2), meta (3) and para (4), and designated as CAU2, CAU3 and CAU4, respectively. The antiproliferative effect and their underlying mechanisms were investigated against both breast (MCF-7R) and ovarian (A2780) cancer cell lines in vitro. Methods: Various in vitro assays that were used included MTT, apoptosis, DNA fragmentation, Annexin V, caspases and Human p53 signaling pathway RT² profiler PCR array. Results: CAU2, CAU3 and CAU4 exhibited strong cytotoxicity against MCF-7R (IC₅₀: 8.14 μM, 7.26 μM and 9.03 μM, respectively) and A2780 (IC₅₀: 1.19 μM, 2.28 μM and 0.785 μM, respectively). The compounds were found to induce both intrinsic and extrinsic apoptotic pathways, as supported by data obtained from the human p53 signaling pathway RT² profiler PCR array and caspase assays. They had significantly upregulated several important gene expressions such as p53, p73 and Bax whilst simultaneously downregulated bcl-2, a key anti-apoptotic gene. Downregulation of MDM2 gene was also observed as it serves as the destructive factor for p53 gene. The compounds also inhibited the NF-kB signaling pathway via activation of Lys48-linked polyubiquitination thus led to NF-kB degradation. The accumulation of reactive oxygen species (ROS) indicated ROS generation thus led to the increment of mitochondrial membrane potential (MMP). Consequently, this led to increased cytochrome c releases from mitochondria, as manifested by flow cytometric analysis. Conclusion: CAU2, CAU3 and CAU4 exhibited significant anticancer effects against both breast and ovarian cancer by inducing intrinsic and extrinsic apoptotic cell death, respectively.

Keywords: gold complexes, apoptosis, antiproliferative, p53, MCF-7R
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P2.20
Antioxidant and Antiproliferative Studies of Different Extracts of Ficus deltoidea Jack
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Background: Ficus deltoidea Jack (Moraceae) is a high value medicinal plant in traditional folk medicine. It has been utilised traditionally as medicine to treat many diseases including diabetes, oedema, hepatitis, kidney stone, rheumatism, hypertensive and jaundice. Objective: To study the antioxidant activity and anti-proliferative effects on four different extracts of F. deltoidea in A549 (lung cancer), HPG2 (liver cancer) and MCF-7 (breast cancer) cell lines. Methods: The F. deltoidea leaves were extracted with chloroform, methanol, ethylacetate and butanol separately by simple cold maceration. Total phenolic and total flavonoid content of four crude extracts was determined by colorimetric method. Anti-oxidant activity of all extracts was determined by DPPH and Ferric Reducing assays. Anti-proliferative activity of extracts was measured by colorimetric MTT assay on A549, HPG2 and MCF-7 cell lines. Results: Methanol extract exhibited highest total phenolic, total flavonoid content and highest percentage of free radical DPPH scavenging activity among all the extracts tested. Likewise, the reducing power activity of all four extracts increased with increased in concentrations of the plant extracts. Methanolic extract showed comparatively good anti-proliferative activity against all the cell lines at 48 hours of treatment (IC₅₀ value A549 =111.3 μg/mL, HPG2 =114.6 μg/mL and MCF-7 = 178.1 μg/mL) whereas, butanol and ethylacetate extracts ineffective against all the three cell lines tested (IC₅₀ value > 1000 μg/mL). Conclusion: Methanol extract of Ficus deltoidea exhibited a significant anti-oxidant and substantial anti-proliferative activities against A549, HPG2 and MCF-7 cell lines.

Keywords: Ficus deltoidea, antioxidant, antiproliferative, cell line.
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P2.21
Combination Therapy of Ruthenium(II) Polypyridyl Complex, [Ru(dppz)2PiP]2+ with PARP inhibitor, NU1025 for Cancer Treatment

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Background: Combination chemotherapy of DNA damaging agent with DNA repair inhibitors has been exploited in the treatment of several cancer cell lines. The role of ruthenium (II) polypyridyl complex, [Ru(dppz)2PiP]2+ (dppz = dipyridophenazine, and PiP = 2-phenylimidazo[4,5-f][1,10]phenanthroline) in anticancer therapy has been studied where it was shown to immediately stall replication fork progression in human cancer cell, leading to DNA double-strand break (DSB) and the initiation of DNA damage response (DDR). This generates interest in exploring the combination treatment of RuPIP with NU1025; an inhibitor of Poly ADP-ribose polymerase (PARP) to enhance the efficacy of RuPIP in cancer treatment. Methods: The anti-proliferative effects of RuPIP and NU1025, alone or in combination on MCF7, T24 and A549 cells were determined by MTT assay and the combination index (CI) values were calculated based on the established method. Cell survival ability was investigated using clonogenic survival assay and cell cycle distribution and apoptosis were assessed by flow cytometric analysis. Results: Treatment with RuPIP alone led to dose- and time-dependent decreases in cell viability meanwhile NU1025 exhibited mild effect on cells as single-agent. CI values < 0.9 was interpreted as synergism and our results showed that the RuPIP-NU1025 combination gave synergistic effects on cancer cells and synergy was further confirmed as combined RuPIP-NU1025 caused total loss in clonogenic potential. Combination treatment also caused a slight increase in G2/M arrest and increase in apoptotic cell death in comparison to control. Conclusion: These finding demonstrates promising therapeutic potential of RuPIP in combination with NU1025 to improve its efficacy in cancer cell killing.

Keywords: Ruthenium Polypyridyl Complex, Cancer, PARP inhibitor, Synergism, NU1025

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P2.22
Cytotoxic activity-guided fractionation of Synclisia scabrida Miers ex Oliv. root and effect of methanolic crude extract on cell cycle progression

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Background: Cancer treatment remains a great challenge to both patient and physicians given the failure to achieve a total cure. As part of the effort in addressing this problem, this study assessed the anticancer activity of Synclisia scabrida (SS) Miers ex Oliv. root and its subfractions against four cancer cell lines and determined the effect of the crude methanolic (MeOH) extract on cell cycle progression. Methods: The air-dried whole root of SS was sequentially extracted with hexane (HeX), dichloromethane (DCM), ethyl acetate (EA) and MeOH, by cold maceration. Preliminary phytochemical analysis was done using standard methods. MTT cell viability assay was performed to assess the in vitro growth inhibition of crude extracts, fractions and subfractions against cancer cell lines [HCT-116 (colon), PC-3 (prostate), MCF-7 (breast), PANC-1 (pancreas)] and to determine the selectivity index (SI) of MeOH extract and SF30 using normal Beas-2B lung cell line. Flow cytometry was used to analyse the cell cycle distribution of control and treated cells. Results: The phytochemical analysis revealed the presence of alkaloid, tannin, steroid, and protein. PANC-1 (IC50 = 5.7 ± 1.2 µg/mL) was the most
sensitive cell line to MeOH extract. The MeOH extract was selectively (SI = 2.6) cytotoxic towards this cancer cell line when compared to HCT-116 (SI = 0.6), PC-3 (SI = 0.5) and MCF-7 (SI = 0.4). EA extract showed the highest SI (3.7) against PANC-1 cells but with the lowest yield. SF30 was most active against PANC-1 cells (26.7±10.4 µg/mL). Just like gemcitabine, SS methanolic crude extract also induced S-phase cell cycle arrest in PANC-1 cells. **Conclusion:** PANC-1 cancer cell line was most sensitive to both the MeOH crude extract and its subfraction (SF30). MeOH crude extract works by arresting cell cycle at S phase. Work is presently in progress to isolate and identify the active anticancer compound(s) present in this plant.

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**P2.23**

**An Andrographolide Derivative Modulates Autophagy in CAPAN-2 Cells**

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**Background:** Autophagy is an intracellular self-degradation mechanism that destroys damaged organelles and proteins in order to maintain normal cellular development and homeostasis. It plays an important role in the modulation of cancer development and in the determination of refractory response to various anticancer chemotherapies. 3,19-(3-Chloro-4-fluorobenzylidene) andrographolide (SRJ23), a new semisynthetic derivative of andrographolide (AGP), was proven to selectively kill pancreatic ductal adenocarcinoma (PDAC) cells. Here, we explored the potential of SRJ23 in modulating autophagy in Capan-2, a pancreatic cancer cell line. **Methods:** 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay was used in assessing the growth inhibition of SRJ23 alone and in combination with chloroquine (an autophagy inhibitor) or rapamycin (an autophagy inducer) against Capan-2 cells. Drug combination effect was determined by Compusyn software. The expression autophagy-related markers, beclin-1, ATG12 and LC3B, was detected by immunoblotting. **Results:** Combination of SRJ23 with chloroquine or rapamycin showed antagonistic growth inhibitory effects. The significant antagonistic effect of SRJ23 was observed at 1-10µM with either chloroquine (10µM) or rapamycin (10µM). SRJ23 induced autophagy but chloroquine significantly inhibited SRJ23 activity by reducing the expression of autophagy markers, beclin-1, ATG12 and LC3B. Contrarily, SRJ23 suppressed autophagy inducing effect of rapamycin, hence leading to reversal of growth inhibitory effect. SRJ23 combined with rapamycin decreased the expression of beclin-1, ATG12 and LC3B, proving that SRJ23 inhibited autophagy. **Conclusion:** The findings suggested that SRJ23 regulates autophagy in promoting cell death of Capan-2. However, whether it promotes or suppresses autophagy, is much dependent on the types of autophagic modulators that are present.

**Keywords:** SRJ23, drug combination studies, autophagy, inhibitor, inducer

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**P2.24**

**Protein Degradation Pathway Inhibition Enhances the Growth Inhibition of Doxorubicin in Breast Cancer Cells**

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**Background:** Two protein degradation pathways exist to degrade intracellular proteins, namely the ubiquitin–proteasome system (UPS) and autophagy. Following anticancer treatments, autophagy acts either as a cytoprotective mechanism to endure therapy-induced stresses or augment cell death induced by anticancer agents. Doxorubicin-containing cytotoxic chemotherapy, the mainstay for the treatment of triple-negative breast cancer, generally yields unsatisfactory outcomes due to its severe cardiotoxicity.
and chemoresistance. In recent years, emerging evidences has implicated that UPS and autophagy are the chemoresistance mechanisms in breast cancer treatment. Proteasome inhibitor (ixazomib) has been reported to enhance the therapeutic effects of doxorubicin in breast cancer cells. However, the role of autophagy in breast cancer cells co-treated with doxorubicin and ixazomib remains unclear. Thus, the present study aims to investigate the role of autophagy in breast cancer cells co-treated with doxorubicin and proteasome inhibitor. **Methods:** The synergistic effect of hydroxychloroquine in combination with doxorubicin and ixazomib was determined by cell viability assay (MTT assay). MDA-MB-231 and MCF-7 cells were treated with a range of concentrations of doxorubicin and ixazomib with fixed concentration of hydroxychloroquine (5µM). The combination index (CI) was calculated using the CompuSyn Software. **Results:** Cell viability assays demonstrated that the triple combinations achieved strong synergism (CI=0.128) and synergism (CI=0.693) on MCF-7 and MDA-MB-231 cells, respectively. Our findings revealed that the autophagy induced by doxorubicin and ixazomib co-treatment serves cytoprotective role in breast cancer cells and the inhibition of autophagy by hydroxychloroquine chemosensitizes breast cancer cells to doxorubicin and ixazomib co-treatment. **Conclusion:** These findings support the strategy of inhibiting both the UPS and autophagy to enhance the efficacy of conventional chemotherapy for breast cancer.

**Keywords:** Autophagy, ubiquitin-proteasome system, doxorubicin, breast cancer, combination therapy

**P2.25**

**Antioxidant Quercetin for Targeted Drug Delivery**

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**Background:** Breast cancer is one of the common cancers in the world and possibility of this disease among women is higher. Literally, women that has been diagnosed with breast cancer may lost their lives when diagnosed at metastatic (advanced) stage since it has highest mortality rate. Drug delivery refer to the technology that has been used up to present the drug to the targeted body site for drug release and absorption. In recent years, variety of nanoparticles have been discovered and synthesized in such way to increase the therapeutic efficiency of drugs through targeted area of tumor cells without causing any harm towards healthy tissue. Thus, it is really fundamental to have a drug-loaded micelles that sustain the drug at certain period of time after administration in order to have a successful drug delivery. Quercetin is a polyphenolic compound that exist in plants, fruits, and vegetables that widely being used in pharmacological applications as showed numerous of positive promising health benefits however, therapeutic applications of quercetin is limited due to its low water solubility and poor bioavailability.

**Objective:** The main objective of this study was to synthesize and characterize quercetin- loaded folic acid-vitamin E TPGS micelles. **Methods:** Vitamin E TPGS micelles containing quercetin were prepared by solvent casting method and were characterized for their particle size, polydispersity (PDI) and surface morphology. Particle size and polydispersity were analyzed using Zetasizer. The surface morphology was determined by performing transmission electron microscopy (TEM) analysis. **Results:** It was observed that the particle size of quercetin-loaded FA- TPGS were less than 20.0 nm and PDI was less than 0.250. From TEM results, it can be observed that quercetin-loaded FA-TPGS micelles were in spherical shape. **Conclusion:** From the findings, it can be concluded that polymeric micelles of quercetin-loaded folic acid-vitamin E TPGS has been successfully formed with smaller particles size and a lower PDI value for targeted drug delivery.

**Keywords:** quercetin, breast cancer, micelles, vitamin E TPGS, drug delivery

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**P2.26**

**Anti-Proliferative Activity of Rhizophora Stylosa Leaves against Oral Cancer (ORL-207) Cell Line (In-Vitro Study)**

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¹1st MACR SCIENTIFIC CONFERENCE 2019
Background: Malaysia is one of the tropical rainforest countries, which consist of different natural resource with significant purpose including herbal plant as medicine source and used in traditional preparations to prevent and treat various types of cancers. Oral cancer is uncontrolled growth of cells in the oral cavity and pharynx due to different factors and complication of oral cancer chemotherapy treatment is likelihood with toxic effects. In view of this, search for alternative products continues and natural plant extracts were consider as good alternatives for the treatment of oral cancer. The plant *Rhizophora* species is a mangrove plant that grows in coastal regions in limited areas in Malaysia and different parts of plants are traditionally been used by local people as a source of for folk medicines commonly to treat infections and variety of ailments like antiseptic and diarrhoea, dysentery, fever, malaria and leprosy. Methods: This research aims to study the anticancer property of organic extracts (petroleum ether, chloroform and methanol) of *R. stylosa* leaves against ORL-207 oral cancer cell line at different concentrations by using MTT assay and evaluated for phytochemical analysis. Results: The results showed that methanolic extracts exhibit anti-proliferative activity at IC₅₀ of 45 μg/mL, while chloroform and petroleum ether extracts are devoid of activity. At the lowest concentration, the extracts did not showed any changes in the percentage of cell viability and at 50 μg/mL methanolic extract showed 44.99% cell viability while other organic extract did not shown any significant reduction in the cell viability. It could be explained by the presence of high percentage of flavonoids and tannins in the methanolic extract of *R. stylosa* leaves. The qualitative phytochemical analysis showed the presence of alkaloids, flavonoids, tannin, glycoside, saponin and terpenoids. Conclusions: Among the different organic solvent extracts tested, methanolic extract of *R. stylosa* leaf showed highest percentage of anti-proliferative activity.

Keywords: *R. Stylusa*, leaves, oral anticancer, anti-proliferative activity, MTT assay
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P2.27
Quinone-Rich Fraction of *ARDISIA CRISPA* Roots (PRIMULACEAE) alters Angiogenic Cascade in Collagen-Induced Arthritis in Rats

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Background: Rheumatoid arthritis is a chronic autoimmune inflammatory joint disease characterized by excessive angiogenesis. Targeting angiogenesis in rheumatoid therapy using plant-derived compounds offers a promising strategy. *Ardisia crispa* or “Mata Itik” in Malay is a traditional herb consumed by local folks as salads and for relieving ailments, including inflammatory rheumatism. The plant roots are enriched with phytochemicals such as saponins, triterpene, flavonoid, tannin, and benzoquinone. Quinone-rich fraction (QRF) isolated from the plant roots exhibits a significant anti-inflammatory, anti-angiogenic, and anti-tumor effect as evidenced. However, the anti-arthritic effect of QRF in angiogenesis implicated arthritic condition remains uncovered. Therefore, the present study investigated the activity of QRF against angiogenesis in collagen-induced arthritis in rats. Methods: Adult male Sprague-Dawley rats were randomly divided into groups: Vehicle control, arthritic control, positive control (celecoxib 5 mg/kg), and treatments (QRF 3, 10, and 30 mg/kg). Arthritis was subcutaneously induced using 150 μg of bovine type II collagen emulsified in incomplete-Freund adjuvant at the base of tail on day 0. The rats were treated orally with 3, 10, and 30 mg/kg body weight of QRF from day 14 to day 26. After 26 days, proteins from synovial joint homogenates were assayed using MILLIPLEX® MAP Multi-Pathway 9-plex Magnetic Bead Signaling kit, phosphoprotein, using Luminex® system and ELISA kits targeting rat VEGF-A and PI3Kα, respectively. Results: QRF significantly reduced VEGF-A, PI3Kα, Akt, NFκβ, p38, STAT3, and STAT5 in various degrees of dosages as compared to arthritic control (p<0.05). Noteworthily, significant anti-arthritic effects were observed even at the lowest dose used (3 mg/kg). However, suppression of these proteins was not in a dose-dependent manner. Conclusion: These findings revealed the potential of QRF as anti-arthritic agent by suppressing multiple proteins involved in angiogenesis in collagen-induced arthritis rat. Further
analysis of these proteins via transcription of their respective DNA, may further verify their exact pathways.

**Keywords:** quinone-rich fraction; Ardisia crispa roots; angiogenesis, rheumatoid arthritis, collagen-induced arthritis rat

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**P2.29**

**SRJ23 Suppresses Growth of Gemcitabine-Resistant Pancreatic Cancer Cells Likely by Inhibiting Autophagy**

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**Background:** Pancreatic ductal adenocarcinoma (PDAC) is currently the fourth leading cause of cancer death globally due to late diagnosis and poor prognosis. Mutation of Kirsten-Ras (K-Ras) oncogene is prevalent in pancreatic cancer patients as more than 90% of patients express the mutation. PDAC is aggressive and lethal as patients developed remarkable resistance to available conventional chemotherapy such as gemcitabine in a short exposure period. SRJ23 (3,19-(3-chloro-4-fluorobenzylidene andrographolide), DCAI (2-(4,6-dichloro-2-methyl-1H-indol-3-yl)ethanamine), selumetinib (MEK1/2 kinase inhibitor) and ulixertinib (Erk1/2 kinase inhibitor) were found to inhibit K-Ras-MAPK oncogenic signalling. In the current investigation, these RAS-MAPK inhibitors were evaluated for their growth inhibition inducing potential in relation to autophagy regulatory proteins against PANC-1 (K-Ras G12D mutation) and Gemcitabine-resistant PANC-1 (P1GR-3.5 µM) pancreatic cancer cell lines. Methods: *In vitro* cytotoxic activity was assessed at 96 hours using MTT cell viability assay. Immunoblotting protocol was carried out to detect autophagy regulatory proteins such as Beclin-1, ATG12 and LC3B. Results and Discussion: As compared to the other RAS-MAPK inhibitors, SRJ23 displayed highest activity in inhibiting cell growth of PANC-1 parental and PIGR-3.5 µM cells with IC₅₀ values of 4 µM and 7.5 µM, respectively (resistant ratio of approximately 2). Immunoblotting of autophagy regulatory proteins in resistant cells revealed high expression of free ATG12 and Beclin-1, both of which are associated with the formation of pre-autophagosomal structures. As an indication of autophagosome formation, low levels of ATG5-ATG12 conjugates were expressed in resistant cells due to the conjugate dissociation after autophagosome formation. This correlates with LC3-I that has lower expression and higher expression of lipidated LC3-II as it associates to inner and outer membrane of autophagosomes after conjugation to phosphatidylethanolamine. Conclusion: From this preliminary investigation, we propose that autophagy seems to promote the survival of gemcitabine-resistant pancreatic cancer cells. These findings implied that SRJ23 induced growth inhibition of cells very likely by mediating autophagy inhibition. Currently, further studies are in progress to confirm our findings.

**Keywords:** autophagy, RAS-MAPK inhibitors, andrographolide derivative, gemcitabine-resistant pancreatic cancer cells

**P3.3**

**Development of Nanostructured Lipid Carriers for Delivery of Methotrexate: A Hyperthermia Approach for Breast Cancer Treatment**

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**Background:** Methotrexate (MTX), a chemotherapeutic agent commonly used for breast cancer treatment, has limited clinical applications and exhibited adverse side effects due to the poor water solubility, non-specific targeting. To overcome the shortcomings, this study has developed a drug delivery system that may enhance the delivery and efficacy by co-encapsulating MTX with a hyperthermic-inducing device known as superparamagnetic iron oxide nanoparticle (SPION) in nanostructured lipid carrier (NLC). Methods: The nano-formulation of MTX-SPION co-loaded NLC was produced by hot ultra-sonication method. The physicochemical characteristics such as particle size,
polydispersity index, zeta potential, encapsulation efficiency of MTX, storage stability and hemocompatibility of the nano-formation were determined. The efficacy of this formulation was determined in MDA-MB-231 breast cancer cells via cell viability, cellular uptake and in vitro magnetic hyperthermic assessments. Results: This multi-modal therapeutic formulation has ideal physicochemical characteristics such as size diameter around 210 nm, polydispersity index less than 0.1, negatively-charged surface, good encapsulation efficiency of MTX (73.1%), stability up to 3 months (25°C) and hemocompatible. The MTX-SPION co-loaded NLC was cytotoxic towards MDA-MB-231 breast cancer cell line in a time-dependent manner with IC50 values of 137 µg/mL and 12 µg/mL at 48 and 72 hours, respectively. The formulation was internalized in the MDA-MB-231 cells via caveolae-mediated endocytosis in a time-dependent manner. Even though the encapsulation in NLC has impeded the hyperthermic behaviour of SPIONs, its weak superparamagnetism was sufficient to cause apoptotic cell death. Conclusion: MTX co-loaded with SPION in the lipid nanoparticle is a potential multi-modal therapeutic regimen for the treatment of breast cancer with enhanced efficacy of MTX. Nevertheless, further in vivo study is needed to understand the pharmacokinetics and magnetic hyperthermic effect of the formulation for clinical translation.

Keywords: Methotrexate, Superparamagnetic iron oxide nanoparticle, hyperthermia, breast cancer, nanostructured lipid carrier

P3.4 The Performing of Hematology Parameter and Electrolyte in Colorectal Cancer

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Introduction: Colorectal cancer (CRC) statistics rates globally, screening can reduced incidence and death. Prevention and early detection are crucial in order to detect cancers at early stages. Altered haematology (Hb, Ht, Platelet count) and electrolyte (Na K, CL) have been found in various cancer types. This study aimed to evaluate the role of haematology and electrolyte as potential biomarkers for the diagnosis of colorectal cancer (CRC), and to assess the association between haematology and electrolyte in CRC clinicopathological characteristics. Methods: This is a cross sectional study of hematology routine and electrolyte of 30 patients in CRC. Data collected were done with Shapiro-Wilk normality test, and Pearson correlation test. Results: The Pearson correlation test for Na obtained very strong negative correlations with Hb (r=-0.825; p=0.000) and strong negative correlations with Ht (r=-0.727; p= 0.000); From the results of the Pearson correlation test for K obtained moderate positive correlations with platelet (r=0.420; p=0.021). From the results of the Pearson correlation test with Cl obtained moderate negative correlation with Hb and Ht (r=0.526; p=0.003, and r=-0.438; p=0.016, respectively). Conclusions: Haematology and electrolyte might play a role in the progress of CRC. Suggested that haematology routine and electrolyte might be a potensial biomarker in the management CRC patients.

Keywords: Hematology, Hb, Ht, platelet count, electrolyte, Na, K, CL, CRC

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P3.5 Establishment of Nasopharyngeal Carcinoma Xenografts: Quality control assessment of fresh tissue specimens collected from hospitals in Malaysia

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Results: From the results of the Pearson correlation test with Cl obtained moderate negative correlation with Hb and Ht (r=0.526; p=0.003, and r=-0.438; p=0.016, respectively). Conclusions: Haematology and electrolyte might play a role in the progress of CRC. Suggested that haematology routine and electrolyte might be a potential biomarker in the management CRC patients.

Keywords: Methotrexate, Superparamagnetic iron oxide nanoparticle, hyperthermia, breast cancer, nanostructured lipid carrier

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Association of autophagy with KRAS mutation and clinicopathological variables and its prognostic value in colorectal cancer patients

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**Background:** Autophagy is a host defensive mechanism responsible of eliminating harmful components through lysosomal degradation. Autophagy has been known to either promote or suppress various cancers including colorectal cancer (CRC). KRAS mutation is an important predictive marker for epidermal growth factor receptor (EGFR)-targeted therapies in CRC. However, the relationship between autophagy and KRAS mutation in CRC is not well studied. This single-centre study aimed to investigate the association of autophagy with KRAS mutation and other clinicopathological parameters, and the potential of autophagy as prognostic marker. **Methods:** Paraffin tissues from 90 CRC patients along with their clinicopathological data were collected and KRAS mutation was determined by qPCR following FFPE DNA extraction. H&E staining was performed on 48 tissues and the expression of autophagy effectors (p62, LC3A and LC3B) was examined by immunohistochemistry (IHC). The outcomes of KRAS mutation and autophagy expression were then associated with the clinicopathological variables. The prognostic value of KRAS mutation and autophagy effectors was then evaluated by Kaplan-Meier survival analysis. **Results:** Cohort analysis showed that Indonesian (51%) has higher KRAS mutation rate than Malaysian Chinese (33%). Our findings demonstrated that the female CRC patients have higher tendency in developing KRAS mutation in Malaysian Chinese population (p<0.05). Out of the three autophagy markers, LC3A was highly associated with the tumour grade in CRC (p<0.05) but not with other clinicopathological parameters. Interestingly, all three markers were highly expressed in the colonic ganglion cells in both cancer and adjacent non-cancer tissues. Lastly, the survival analysis did not yield any statistically significant outcome. **Conclusion:** This study concluded that KRAS mutation
and autophagy effectors are not good prognostic markers for CRC patients. Furthermore, our findings showed that autophagy expression was not cancer- and tissue type-specific, suggesting that this process can be complex and multifactorial which require future investigation.

**Keywords:** Autophagy, KRAS mutation, colorectal cancer, prognostic marker, Malaysia.

**P42**

**PD-L1 Expression in Non–Small Cell Lung Cancer in HTAA: A retrospective study**

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**Background:** Programmed death ligand (PD-L1) TPS (tumour proportion score) on tumour cells have been showed to play a major role in determining the response of immunotherapy in non-small cell lung cancer (NSCLC). However, most centre do not perform this test routinely in Malaysia. This is because most of our patients cannot afford immunotherapy. We routinely performed PD-L1 TPS in all patients with NSCLC since this test was available in Malaysia. **Methods:** A retrospective study consists of 131 patients diagnosed with NSCLC from January 2017 to September 2019 were recruited at our study. Surgical resection specimens, small biopsy (transbronchial, endobronchial, core needle or pleural biopsy) samples, and cytologic cell blocks (needle aspirates or pleural fluid) were tested. Samples were analysed for PD-L1 TPS by using the clone 22C3 pharmDx kit and were classified into ≥50%, 1-49% and <1%. PD-L1 expressions were analysed between patients with or without driver mutation and another clinical demographic. **Results:** Among them, 67.2% were male and majority were Malays (66.4%) and Chinese (30.5%). 56.8% were smoker or ex-smoker. 28.2% had PD-L1 TPS of ≥50% and 43.5% had negative PD-L1 TPS (<1%). EGFR mutation were seen in 37.7% of patients and majority are 19 deletion and L858R mutation. ALK rearrangement was seen in 6.6% of patients. Patients without driver mutation are more likely to have positive PD-L1 expressions, but it is not statistically significant (59.3% vs 40.7%, p=0.231). 60.0% of smoker or ex-smoker had positive PD-L1 TPS as compared to 40.0% of non-smoker (p=0.266). No significant correlation was seen between PD-L1 TPS positivity with patient sex, race, ECOG functional status or tumour stage. **Conclusion:** PD-L1 expression is seen in 56.5% of patients with NSCLC especially in smoker or ex-smoker and patients without driver mutation.

**Keywords:** PD-L1, Programmed Death Ligand 1, Non-Small Cell Lung Cancer, Malaysia, Driver Mutations

**P51**

**Prevalence of burnout among the house officers in Ibrahim Malik Teaching Hospital, Khartoum –Sudan, 2019**

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**Background:** Burnout is a psychological syndrome of emotional exhaustion, depersonalization and reduced personal accomplishment. It can cause a deleterious impact on doctors causing intent to quit medical practice, intention to leave the current position, and poor health. It can also negatively affect the quality of patient care, and decrease patient safety. **Objectives:** The objectives of the study were to assess the prevalence of burnout among the house officers, identify the factors affecting burnout among the house officers and compare the prevalence of burnout in different specialties of Ibrahim Malik teaching hospital. **Methods:** This cross-sectional study was conducted at Ibrahim Malik teaching hospital in July 2019 among house officers. Data was collected through written questionnaires. Analysis was carried out using Statistical Package for the Social Sciences (SPSS), version 26. **Results:** From all enrolled respondents, 52 were house officers, 46.2% scored high for emotional exhaustion burnout, 92.4% for depersonalization and 65.4% for personal accomplishment. The factors affecting the burnout score included women gender, marital status,
medical specialty, sleep deprivation and smoking. The highest prevalence (42.3%) was reported in medicine department house officers. **Conclusions:** The prevalence of burnout among the house officers was high in Emotional Exhaustion burnout score, Depersonalization and Personal Achievement scores. Multiple factors can affect the burnout score; therefore, further multicenter studies should be conducted to reiterate these results.

**Key words:** burnout, emotional exhaustion, depersonalization, personal accomplishment

**P52**  
**Effect of coffee consumption and risk of esophageal carcinoma in Kassala State, Eastern Sudan 2019**

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**Background:** In epidemiologic studies, association between coffee consumption and esophageal cancer risk is inconsistent. **Objective:** The aim of study was to evaluate the effect of coffee on esophageal cancer by combining several similar studies. **Methods:** We conducted a Cross section for association of coffee intake and esophageal cancer incidence. Eleven studies, including 1010 participants and 865 incident cases, were identified. A relative risk (RR, for cohort study) or odds ratio (OR, for case–control study) of heavy coffee drinkers was calculated, compared with light coffee drinkers or non-drinkers. The analysis was also stratified by cancer types (esophageal squamous cell carcinoma and esophageal adenocarcinoma), sex, and geographic region. **Results:** The summarized OR of having esophageal cancer in heavy coffee drinkers was 0.93 (95% confidence interval: 0.73–1.12), compared with light coffee drinkers. When stratified by sex, pathologic type of esophageal cancer, and type of epidemiologic study, we did not find any association of coffee consumption and esophageal cancer incidence. However, an inverse association between coffee consumption and incidence of esophageal cancer was found in Beja tribes' participants in Kassala with OR of 0.64 (95% CI: 0.44–0.83), but not in Africa participants (OR = 1.05; 95% CI: 0.81–1.29). **Conclusion:** There is a protective role of coffee consumption against esophageal cancer in Kassala state Sudan, but not in African.
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WGS approaches can be used to comprehensively explore all types of genomic alterations in cancer and help us to better understand the whole landscape of driver mutations and mutational signatures in cancer genomes and elucidate the functional or clinical implications of these unexplored genomic regions and mutational signatures. This approach combined with mathematical analysis and other omics analysis can clarify the underlying carcinogenesis and achieve molecular sub-classification of cancer, which facilitates discovery of genomic biomarkers and personalized cancer medicine.

DNA is randomly fragmented by physical shearing, and 30-50x sequence depth (90-150 Gb) of each human whole genome is usually sequenced for both cancer and normal genomes, which can cover 99% of the entire human genome.

About 5 to 10 percent of all cancers are caused by known inherited gene mutations. These mutations are passed down from generation to generation. Through WGS, patients are able to assess their risk for many types of cancer, including kidney, skin, lung, breast, ovarian, colon, endocrine, prostate cancers and etc. If a known genetic predisposition to cancer is found, a physician or genetic counselor is able to counsel the patient about the best ways to detect early cancers or, better yet, prevent cancers from ever forming.

Who can benefit from WGS?

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Cancer genes can be grouped into two classes: class I genes are mutated or deleted; whereas class II genes are not altered at the DNA level, rather their expressions at RNA level are affected, and the effects are reflected at the phenotype. Conventionally, in the study of diseases like cancer, only mutated (class I) genes have been considered as candidate cancer genes, cancer genes of class II have been neglected by cancer geneticists. Until now, the focus has been on class I genes and the screening methods have been largely limited to searches for alterations in DNA.

But cancer phenotypes result from altered RNA expression (class II), and there is no simple 1:1 relationship between mutated genes and cancer phenotypes. Therefore, it's not enough to know whether a gene is mutated or normal - it's also important to know whether the gene is expressed and how it is expressed.

In general, a DNA test and an RNA test serve to provide different genetic data. The genetic data acquired from a DNA test is static, but an RNA test provides dynamic data. Repeated tests in DNA do not provide different results, but in RNA, it does. This is because DNA doesn't change with external factors, but RNA expression changes with lifestyle and environmental factors. Hence, a DNA test measures the lifetime risk of diseases, but an RNA test measures those risks for the present.

By utilizing the molecular barcoding technology, MyGenome is able to investigate 770 gene expressions that combine vital components involved in the complex interplay between the tumour, microenvironment and immune response in cancer. Both over-expressed and under-expressed genes can be identified in a single test, making it possible to recognize genes whose expression changes during development, carcinogenesis, or any other processes under investigation.
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• Next Generation Sequencing (NGS)
Whole genome sequencing is carried out to produce a complete set of genetic data, including coding and non-coding regions of DNA, in order to identify genetic variants not just within the exon regions, but intron regions as well. Studies have found out that approximately 15% of disease-causing variants are found in the non-coding regions, and the whole exome sequencing (WES) method would not have been able to detect them. This is because WES only covers the protein coding sequences, which only consist about 1% of the entire genome. While WES does cover most of the protein coding regions, WGS provides a complete coverage, detecting mutations in promoter regions, enhancers, suppressors, etc.

At My Genome, we utilise the DNaseq™ technology to perform WGS. DNA fragments are amplified via Rolling Circle Amplification (RCA) to produce DNA nanoballs. Each amplicon is produced based on the original template, hence there will be low amplification bias and no error accumulation. This allows us to produce accurate data with 99.9% SNP precision/sensitivity and 99% indel precision/sensitivity. We also utilise a patterned array, whereby each spot on the flow cell is uniformly shaped and distanced. This allows high imaging efficiency, high density, high sequencing accuracy, while low duplicate rate and no index hopping. Lastly, the cPAS chemistry is used to incorporate a fluorescent probe to a DNA anchor on the DNB, followed by high-resolution digital imaging.

• Digital RNA Counting
When gene expression profiling was introduced, it allowed scientists to reliably detect cancer formations at their early stages, increasing the chances of survival in cancer patients. However, the conventional methods of gene expression profiling require the conversion of mRNA transcripts to cDNA, followed with PCR amplification, and as with PCR amplification, production of biased data is often the major problem, which would lead to unrepeatable results.

At My Genome, we perform gene expression profiling with a digital counting technique. Conversion step of RNA to DNA is removed, instead RNA is tagged and counted at its native level, with a patented molecular barcoding technology. Therefore, there will be no PCR bias and error, producing highly reproducible results.

• Real-Time PCR
Quantitative PCR, or real-time PCR, is an evolution to the conventional PCR amplification as quantification of amplicons can be monitored during the amplification process instead of after the PCR reaction. The ability to measure amplicons during the exponential phase of the PCR amplification removes the post-PCR processing step, thus data is produced at higher precision, sensitivity, and resolution. It is becoming the gold standard test for accurate, sensitive and fast diagnosis for a large range of infectious agents. It is widely used for detection and quantification of chromosomal translocations and viral load, to monitor minimal residual disease after treatment and to show graft-versus-lymphoma effects.
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