MEETING OF MINDS IN CANCER RESEARCH

ASCOMOS 2019

CRM SCIENTIFIC SESSION

2ND NOVEMBER 2019

9:00 AM - 4:45 PM

LECTURE HALL 3

CRM
CLINICAL RESEARCH MALAYSIA
Your Global Solutions in One Nation

Malaysian Oncological Society

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ABOUT CLINICAL RESEARCH MALAYSIA

Clinical Research Malaysia (CRM) exists to advance global health solutions for a brighter, more hopeful future for the people by providing speedy and reliable end-to-end clinical research support for quality studies. As these studies unfold, we work together with our partners to create an impetus in delivering better treatment to our end consumers, while at the same time creating high-skilled job opportunities.

The strength of our operation lies in our innate understanding of the local clinical research landscape and implementation of international standards. This, when considered in parallel to the fundamental backing of the government ministries, provides us with an incomparable advantage, as we work hand-in-hand with our partners from the nascent stages of development to materialisation of the end product.

In the journey towards a brighter and better future, we facilitate the entry of industry-sponsored research into Malaysia, working closely with the government and relevant authorities to ensure that all regulations and best practices are met.

In CRM, we credit the outstanding performance to the team we have anchored from within our organisation. Their endless pursuit of innovation and continuous improvement have propelled CRM forward to optimise the opportunities that come our way. In tandem with our passion for the clinical research landscape, we ensure core values of transparency, honesty, accountability and trustworthiness resonate throughout CRM. These qualities are also cascaded to our principal investigators and Study Coordinators, who act as the catalysts of the clinical research process.

As CRM vouches for an aspiring future in the clinical research industry, we have implemented mechanisms to expand hospital capacity for clinical trials and tests. This is possible by tapping into our vast talent pool consisting of principal investigators and medical assistants.

CRM'S SCOPE OF SERVICES

CRM currently provides the following services:

Feasibility Studies & Investigator Matching

Development & Placement of Study Coordinators

Consultation and Management of Clinical Trial Budget

Review of CTA & NDA

One-stop Centre for the Industry

Improving Public & Patient Awareness

Promoting Malaysia as a hub for Industry Sponsored Research (ISR)

Growing the pool of investigators and sites

Training related to Clinical Research

Sites capability improvement & enhancement

PROGRAMME

Time	Programme	Speaker
8:30 – 9:00	Registration	
9:00 – 9:45	Short Oral Communication	
9:45 – 10:15	Tea Break and Booth Interaction	
10:15 – 12:00	Symposium: Genomics and Biomarker Research	Chairperson: TBC
10:15 – 10:35	Are breast cancers in Asians different - lessons from genomic and transcriptomic profiling of 576 Malaysian breast cancers	Prof Datin Paduka Dr Teo Soo Hwang (Cancer Research Malaysia)
10:35 – 10:55	Are biomarkers in Asian cancer patients different - Challenges of Biomarker Research in Malaysia from a Pathologist's Perspective	Dr Ch'ng Ewe Seng (USM)
10:55 – 11:15	Mass Spectrometry Imaging In Cancer Biomarker Discovery	Prof Dr Gurjeet Kaur (USM)
11:15 – 11:35	CRC research in UMBI - paving the ways for precision medicine in Malaysia	Dr Nurul Syakima Ab Mutalib (UKM)
11:35 – 12:00	Q&A	
12:00 – 14:00	Lunch and Booth Interaction	

PROGRAMME

Time	Programme	Speaker
14:00 – 14:50	Symposium: Drugs Discovery	Chairperson: Dr Tan Chih Kiang
14:00 – 14:20	2-Methoxynaphthalene-1, 4-Dione Suppresses PKC and Its Down-Stream Transcriptional Factors in Human Burkitt's Lymphoma Cell	Prof Dr Lim Yang Mooi (UTAR)
14:20 – 14:40	Targeting Metabolic Vulnerabilities in Triple Negative Breast Cancer	Associate Prof Dr Ivy Chung (UM)
14:40 – 14:50	Q&A	
14:50 – 16:00	Symposium: Awareness, Early Diagnosis and Improved Survivorship	Chairperson: Prof Esther Ebenezer Gunaseli
14:50 – 15:10	Cancer Survivorship: Current status and research opportunities in Malaysia	Associate Professor Nirmala Bhoo Pathy (UM)
15:10 – 15:30	Promoting Awareness of Cancer and Early Detection in Malaysia: A way forward	Prof Dr Tin Tin Su (Monash University)
15:30 – 15:40	Q&A	
15:40 – 16:45	Translational Research Speed Networking	
16:45 – 17:00	Tea Break and Booth Interaction	

Calling all Researchers & Clinicians!

TRANSLATIONAL RESEARCH SPEED NETWORKING

Date: 2nd November 2019
Time: 3:40 pm
Venue: Lecture Hall 3

Don't miss this excellent opportunity to start collaborations between clinical practice and academia

***Limited seats available**

To RSVP, kindly email to asha@clinicalresearch.my

SPEAKERS ABSTRACT

Are Breast Cancers In Asians Different - Lessons From Genomic And Transcriptomic Profiling Of 576 Malaysian Breast Cancers

Professor Datin Paduka Dr Teo Soo Hwang
Cancer Research Malaysia, Malaysia

Breast cancer incidence in Asia is increasing because of changes in reproductive and lifestyle factors. Differences exist between breast cancers in women of Asian and European descent, including younger age of onset and correspondingly, higher prevalence of hereditary factors. Together, these suggest potential crucial differences at the molecular level. Here, we report whole exome sequencing, shallow whole genome sequencing and transcriptomic sequencing on 576 Malaysian breast cancers. Asian breast cancer show higher prevalence of Her2+ molecular subtypes and TP53 mutations, as well as higher immune scores compared with Caucasian breast cancers. These results underlie the molecular differences between Asian and Caucasian breast cancers and point to potential differences in therapy and outcome.

Are Biomarkers In Asian Cancer Patients Different - Challenges Of Biomarker Research In Malaysia From A Pathologist's Perspective

Dr Ch'ng Ewe Seng
University Sains Malaysia, Malaysia

This talk takes the routinely examined breast cancer biomarkers as a case study to address the issue whether these biomarkers in Malaysia are truly different from the others. By extrapolating the challenges to accurately determine the status of these mandatory biomarkers, inherited challenges surmounting discovery and validation of new cancer biomarker will be highlighted. In this regard, this talk will emphasize the roles of pathologists as the guardian of cancer tissue in providing optimal research materials while safeguarding the patients' interest for the best patients' care. Recommendations are made on how to move forward to procure better research materials and accurate baseline cancer parameters for biomarker research.

SPEAKERS ABSTRACT

Mass Spectrometry Imaging In Cancer Biomarker Discovery

Professor Dr Gurjeet Kaur
Universiti Sains Malaysia, Malaysia

Extensive research is done to identify biomarkers for use in early cancer detection, diagnosis, prognosis and monitoring therapeutic responses. There are various platforms to study biomarkers which include genomics, proteomics and metabolomics. Majority of the methods use fresh tissue or bodily fluids and compare differential patterns between normal and cancer. Formalin-fixed paraffin embedded (FFPE) tissues are routinely used for histopathology evaluation and diagnosis in pathology laboratories. They are easily available and provide a source of invaluable material namely DNA, RNA and protein for experiments in biomarker identification. Relatively few models allow spatial information of a biological molecule with preservation of tissue morphology. A sensitive technique, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry imaging (MSI) can acquire a comprehensive proteomic analysis with spatial distribution and intensity of hundreds of peptides corresponding to proteins of interest from a single FFPE tissue section. Mass spectrometry (MS) is performed after antigen retrieval, enzymatic digestion and addition of matrix on a tissue section. In the mass spectrometer, a UV laser strikes the sample, ionizes the peptide sample and sorts ions based on mass to charge ratio. The detectors measure each ion collision producing a spectrum of m/z versus intensity. The m/z values allow peptide and protein identification using a database. Tissue microarrays consisting of hundreds of cancer tissue cores allows a large cohort to be studied using a similar approach. Recent research done by our group headed by Prof. Peter Hoffmann at University of South Australia, showed the value of MALDI-MSI in distinguishing endometrial cancers with and without lymph node metastasis. Specific N- glycans were also identified in different stages of ovarian cancer. An introduction to mass spectrometry imaging and its clinical applications will be shared during the talk.

CRC Research In UMBI - Paving The Ways For Precision Medicine In Malaysia

Dr Nurul Syakima Ab Mutalib
University Sains Malaysia Medical Center, Malaysia

Colorectal cancer (CRC) remains as the third most common cancer worldwide and the incidence is increasing in many parts of the world, including Malaysia. The expected rise in CRC burden in Malaysia underlines the importance of pursuing a deeper understanding of this cancer, particularly at the molecular level. The UKM Medical Molecular Biology Institute (UMBI) has been actively investigating the molecular pathogenesis of CRC to understand its genetic makeup, identify biomarkers for early detection and prognostication, study molecules involved in chemoresistance, and characterise the druggable genes for precision medicine. Most recently, UMBI is involved in an international effort to screen the status of microsatellite instability (MSI) status among our CRC patients. On the translational research front, we have come up with Colopredict, our patent-pending gene panel, which will enable doctors to select which Duke's B and Stage 2 CRC patients who will benefit from chemotherapy. From our whole genome sequencing of CRC patients, at least 1 actionable variant was identified in KRAS, BRAF, PIK3CA, SMAD4 and FBXW7 genes, which are potentially involved in determining responses towards chemotherapeutic drugs such as 5-fluorouracil, cetuximab and panitumumab. In the era of immunotherapy, MSI status is imperative for selecting patients who will greatly benefit from the treatment. These in depth analyses of the molecular signatures illustrate a multidimensional and comprehensive genetic landscape that highlights the complexity of CRC and provides a road map to facilitate genome guided precision oncology in Malaysia.

2-Methoxynaphthalene-1, 4-Dione Suppresses PKC And Its Down-Stream Transcriptional Factor In Human Burkitt's Lymphoma Cell

Professor Dr Lim Yang Mooi
Universiti Tunku Abdul Rahman, Malaysia

Protein Kinase C and its down-stream transcriptional factors, NF-κB and AP-1 are involved in governing cancer cell growth, proliferation, survival, apoptosis, angiogenesis and metastasis. 2-Methoxy-1,4-Naphthoquinone (MNQ) isolated from the pericarps of Impatiens balsamina, Linn, has been studied to show cytotoxicity effects on various cancer cell lines, trigger apoptotic pathway and the upper stream modulator of many cancer pathways, and inhibit protein kinase C expression in Human Burkitt's Lymphoma cells. Owing to its promising anti-tumour effects, further mechanistic studies was continued to investigate whether MNQ could possibly regulate the NF-κB and AP-1 transcriptional factors and COX-2 expression through PMA-induced PKC activation and to study the regulatory effect of MNQ on the key cancer genes in various signalling pathways in Human Burkitt's Lymphoma cells. The findings demonstrated that MNQ suppressed the expression of NF-KB, AP-1 and COX-2 at 36.10 and 34.56 μM (IC50), and 80 μM (IC90), respectively, and it could possibly involve in controlling cell inflammatory responses in Human Burkitt's Lymphoma cells. MNQ was also indicated to regulate other genes that are involved in apoptosis, tumour suppressor and cell cycle regulation. This study demonstrates that MNQ possesses regulatory effects on the abovementioned genes and could contribute to the suppression of carcinogenesis in human Burkitt's lymphoma cells.

SPEAKERS ABSTRACT

Targeting Metabolic Vulnerabilities in Triple Negative Breast Cancer

Associate Professor Dr Ivy Chung
University of Malaya, Malaysia

Triple negative breast cancer (TNBC) is considered to be more aggressive and have a poorer prognosis than other subtypes of breast cancer. Their growth are not fueled by the hormones estrogen and progesterone, and HER2 ligands. Thus, metabolic reprogramming may be key to the aggresive cell growth and survival in TNBC. Fatty acid binding protein 7 (FABP7), a lipid trafficking protein, is predominantly expressed in TNBC tumours, and is associated with longer survival. However, the mechanistic action of FABP7 in regulating the metabolism of TNBC remains unknown. Ectopic expression of FABP7 in TNBC cell line Hs5778T cells cultured in serum-starved condition leads to increased cell death, likely due to cell cycle arrest in S/G2 phase. A significant change in gene expression of enzymes involved in glucose-, glutamine- and fatty acid-metabolism were observed in these cells. Serum starvation-induced cell death in FABP7 overexpressing TNBC cells was potentially regulated by peroxime proliferator-activated receptor (PPAR)-α signalling, as the addition of PPARα antagonist led to a full phenotype reversal. Further, when another TNBC cell line MDA-MB-231 cells were treated with linoleic acid, a substantial increase of cell death was also observed, accompanied with a downregulation oflipoxygenase, 15-LOX-1 gene and its product, 13-HODE. This phenotype was attenuated with a rescue treatment using 13-HODE. The decrease in 13- HODE was potentially due to fatty acid partitioning modulated by FABP7, as demonstrated by an increase in fatty acid oxidation. Taken together, FABP7 affected TNBC cell survival by regulating lipid metabolism when fatty acid levels were dysregulated. Our study suggests that metabolic vulnerabilities driven by FABP7 can be explored as potential therapeutic implications, and FABP7 may act as a biomarker for such dependency.

SPEAKERS ABSTRACT

Cancer Survivorship: Current Status And Research Opportunities In Malaysia

Associate Professor Nirmala Bhoo-Pathy
University of Malaya, Malaysia

Findings from the ASEAN Costs in Oncology (ACTION) Study has shown that cancer survivors in Malaysian settings continue to report impaired quality of life and high levels of psychological distress at one year after diagnosis. This appears to suggest that they have many unmet needs. The assessment of needs for cancer care is a critical step in provision of high-quality care and improving the quality of life and well-being of cancer survivors and their families. From a healthcare provider's perspective, inadequate understanding of patient's needs may not only lead to unnecessary suffering to patients and their families, but also increase healthcare costs. Improved understanding on the needs of cancer patients will not only allow healthcare providers to tailor interventions to address patients' needs but also to identify the relevant stakeholders outside the healthcare system to address some of the unmet needs. Between 2017 and 2018, our research group conducted a series of qualitative studies in several hospitals across Klang Valley, aimed at improving our understanding on the needs of men and women living with cancer in Malaysia. In this talk, key findings and policy implications will be presented.

Promoting Awareness Of Cancer And Early Detection In Malaysia: A Way Forward

Professor Dr Tin Tin Su
Monash University, Malaysia

Breast and colorectal cancer are the two most common cancers in Malaysia. There is no population-based cancer screening in Malaysia. Thus, most cancer cases are diagnosed through presentation of symptoms rather than regular screening. Low awareness coupled with stigma and erroneous beliefs delay help seeking behaviours, lead to late presentation and contribute to poor detection rates. Promoting cancer awareness through mass media may be effective in improving cancer-related knowledge and uptake in screening tests. However, research is sparse regarding the cultural translation and implementation of mass media campaigns in Malaysia (and Asia) in terms of raising awareness about colorectal and breast cancer. A collaborative partnership comprising researchers from Malaysia and the UK as well as policy makers, public health experts and non-government organisations from Malaysia was formed to design, deliver and evaluate the Be Cancer Alert Campaign (BCAC). Each awareness-raising campaign ran for five weeks (Colorectal Cancer in April 2018, followed by Breast Cancer in October 2018). Evaluation of the campaigns took place in Gombak district (Colorectal Cancer) and Petaling district (Breast Cancer) respectively, in the form of a pre-post randomly selected household survey and collection of service utilisation data. Over 65% of participants recognised BCAC materials when prompted post-campaign, in particular from TV advertisement and posters in clinics. Age, ethnicity and education were associated with campaign recognition. BCAC recognisers were significantly more likely to be aware of all CRC symptoms (when prompted) at follow-up and were more confident to notice symptoms compared to non-recognisers. The findings suggest an improvement in symptom awareness as a result of the BCAC. Differences between ethnic and age groups suggests that future mass media campaigns need to be further targeted to reduce disparities in campaign reach. Malaysia and most South-East Asian countries have a low middle-income economy, with limited resources for cancer control. Late-staged cancers impose a significant economic burden on patients, households, communities, employers, health systems and governments. Our proposed strategy for the implementation of the culturally sensitive mass media cancer awareness-raising campaign will serve as a blueprint for cancer prevention and control policy in South-East Asian countries where the burden of cancer is increasing and there are high cancer death rates.

PARTICIPANTS ABSTRACT

CRM 01: Psychosocial and Supportive Care for Cancer Patient in Malaysia: Radiation Therapist Perceptions

Nor Aniza Azmi[1] , Rozilawati Ahmad[1] , Farah Nurantasha Rashid[1] , Khadijah Khamsan[2] , Farihan Jaffar[3] [1]School of Diagnostic Imaging and Radiotherapy, Health Science Faculty, Universiti Kebangsaan Malaysia, 50300 Kuala Lumpur, [2]Radiotherapy and Oncology Dept., Hospital Canselor Tuanku Muhriz, Jalan Yaacob Latif Bandar Tun Razak Cheras, 56000 Kuala Lumpur, [3]National Cancer Institute Jalan P7 Presint 7, 62250 W.P.Putrajaya

INTRODUCTION:
Radiotherapy is one of cancer treatment using high energy radiation to kill the cancer cells. The side-effects of radiotherapy can be seen in term of physical and psychological. Radiation therapists (RTTs) are responsible in delivering radiotherapy for cancer patients and potential to deliver psychosocial oncology and supportive care (PSOSC). A study has been conducted to identify the knowledge and perception of RTTS on PSOSC.

MATERIALS METHODS:
The survey consist of 6 baseline and 34 statement questions which is in the form of 8-point Likert scale. Statements were divided into three theme of personal convictions and motivations, professional preparedness and execution and environmental resources and facilitators. The eight-point scale representing their opinion based on the scale given (1 = "strongly disagree" to 8 = "strongly agree").

RESULTS:
A total of 52 RTTs have moderate agreement regarding the understanding of patients and families related to the need for PSOSC with the mean of 5.54 and SD value 1.41. RTTs has a good understanding on the purpose of PSOSC towards cancer patients. The lack of confidence of some RTTs to develop a problem list related to PSOSC can be observed by the result with a mean of 5.65 and SD value 1.30.

DISCUSSIONS:
Majority of respondent aware of the PSOSC importance. Communication skills training is necessary to improve the emotional conversation between RTTs and patient (1). Lack of education regarding emotional distress could affect the comfort level of RTTs during the conversation with cancer patients and 87% of RTTs would like to have profound education in the management of anxiety and depression symptom (2).

CONCLUSION:
Training, facilities, support and initiative from the institution management is needed to improve the ability to help RTTs in delivering better and effective PSOSC.

REFERENCES:
1. van Beusekom, et al. BMJ Open 2019. 9 (4): e025420.
2. Lavergne, C., et al. Journal of Medical Imaging and Radiation Sciences 2015. 46(1): 30-36.

PARTICIPANTS ABSTRACT

CRM 02: Local Experience on Bone Scintigraphy Evaluation of Skeletal Involvement in Paediatric Langerhans Cell Histiocytosis

Ahmad Zaid Zanial, Tejvinder Kaur Sodhi Paritam Singh, Siti Zarina Amir Hassan. Nuclear Medicine Department, Hospital Kuala Lumpur

INTRODUCTION:
Langerhans cell histiocytosis (LCH) is considered a rare immune system malignancy with manifestations ranging from isolated bone lesions to multisystem disease. Bone scintigraphy is an established oncological investigation modality and used to evaluate LCH skeletal involvement especially at centres without positron emission tomography. We aimed to examine clinical characteristics of paediatric LCHs whom underwent bone scans and their scintigraphy findings.

MATERIALS/METHODS:
Retrospective study on whole-body 99mTechnetium-diphosphonate bone scans performed among histology-proven LCHs (≤18 year-old) at Nuclear Medicine Department, Hospital Kuala Lumpur between May 2014 and December 2018. Cases with documented ongoing bone infection or suspicion of concurrent/ other malignancy were excluded. Compiled data and scan findings were analysed using descriptive study and relevant statistical tests.

RESULTS:
52 bone scans involving 20 children were included. Most children (13/20) had ≥2 scans done during the study period. Mean age at first bone scan visit was 4.45 years. Majority were boys (12/20) and had multisystem disease (14/20). During their first visit, 8 children had solitary lesion compared to 11 children with ≥2 lesions. Overall, 42 scans were reported to be abnormal with majority being increased tracer uptake (34/42). Main site of skeletal involvement was skull. Children having ≥2 lesions were significantly associated with skull involvement ($p<0.05$).

DISCUSSIONS:
In children, skull is the most affected bony site with LCH lesions classically demonstrating radiographically osteolytic punched out with sharp margins.[1, 2] Multifocal disease has poorer prognosis whereas head and neck LCHs have higher recurrence.[3]

CONCLUSION:
Our patients were mostly young boys having multisystem disease. Main abnormal scintigraphy was increased tracer uptake lesions. Children with ≥2 lesions had significant association with skull involvement. Attention needed in reporting bone scintigraphy of these high risk cases.

REFERENCES:
1. Morimoto A et al (2014). Recent Advances in Langerhans Cell Histiocytosis. Pediatrics International 56: 451-461
2. Zaveri F et al (2014). More than Just Langerhans Cell Histiocytosis: A Radiologic Review of Histiocytic Disorders. RadioGraphics 34: 2008-2024
3. Buchmann L et al (2006). Primary Head and Neck Langerhans Cell Histiocytosis in Children. Otolaryngology-Head and Neck Surgery 135: 312-317

PARTICIPANTS ABSTRACT

CRM 03: Best-Buys at Government Primary Care: Conventional Pap Smears Versus Liquid Cytology

Narentharen Selvarajah*, Azainorsuzila Mohd Ahad*
*Klinik Kesihatan Lukut, Port Dickson, Ministry of Health Malaysia

INTRODUCTION:
Cervical cancer is the 3rd most common cancer in Malaysian women. 1682 women are diagnosed with cervical cancer and 944 die from it yearly.[1] A population-based screening using the Papanicolaou (PAP) smear is recommended by the national clinical practice guidelines[2]. Smears without endocervical cells are troublesome to both doctor and patient due to delayed detection of disease and increased use of limited resources when repeating the smears[3].

MATERIALS METHODS:
We evaluated all cervical cancer screening done at Klinik Kesihatan Lukut, Port Dickson from 2015 to 2018. We divided them into two cohorts; conventional pap smears(year 2015, N=742) and liquid cytology(years 2016, 2017, 2018, N=1726). The sample collection method and staff who were performing it were unchanged. The outcome was the absence of endocervical cells.

RESULTS:
Endocervical cells were absent in 17.25% of conventional smears. Liquid cytology samples had much lower absence of endocervical cells at 8.98%. (Difference: 8.27 %, 95% CI 5.3425% to 11.4182%, P < 0.0001). Abnormal results were 1.21% for the conventional smears and 2.38% for the liquid cytology(P = 0.0587).

DISCUSSIONS:
Liquid cytology significantly increases the detection of endocervical cells. This would translate into substantial public health savings in terms of cost and manpower as there would be lesser repeat screening and increased early detection of abnormalities.

CONCLUSION:
Liquid cytology for cervical cancer screening is the best buy at busy government primary care settings.

REFERENCES:
1. HPV Information Centre. Malaysia: Human Papillomavirus and Related Cancers Fact Sheet 2018. (2019, June 17). Retrieved October 6, 2019, from http://www.hpvcentre.net/statistics/reports/MYS_FS.pdf
2. Ministry of Health Malaysia. Clinical Practice Guidelines on the Management of Cervical Cancer: 2nd Edition. (2015). Retrieved October 6, 2019, from http://www.moh.gov.my/moh/penerbitan/CPG/QR%20Management%20of%20Cervical%20Cancer%20(Second%20Edition).pdf
3. Sun L, Wang P-H, Lee C-H, et al. Clinical parameters associated with absence of endocervical/transformation zone component in conventional cervical Papanicolaou smears. Taiwan J Obstet Gynecol. 2016;55:81–84.

PARTICIPANTS ABSTRACT

CRM 04: Development of Multifunctional Nanomaterials, Their Delivery and Efficacy as Cancer Cells Extermination

Che Azurahanim Che Abdullah* and Emmellie Laura Albert
Universiti Putra Malaysia, azurahanim@upm.edu.my

INTRODUCTION:
Cancer chemotherapy drug is a powerful drug used to treat cancer. Cancer chemotherapy drugs are not specific on their metabolic pathways to the cancer cell. They suffer from poor tissue specificity and non-specific toxicity. Therefore, current research improved the delivery of chemotherapeutic agents to the cancer cells by applying targeted drug delivery using composite nanoparticles for the targeting chemotherapy drug to increase their effectiveness in treating the unhealthy tissue and thus reduce the general toxicity and avoiding repetitive injection to improve favorable drug pharmacokinetics.

MATERIALS METHODS:
Chemicals were purchased from Sigma-Aldrich. MNPs were synthesized using the co-precipitation method. O/W emulsion technique were applied to encapsulate OAMNPs within PLGA (75:25). The method for the preparation of TAM-loaded magnetic polymeric nanoparticles (TAM-PLGA-OAMNP) was adapted the method of O/W emulsion-evaporation technique. The colloidal stability test is conducted in three separate solutions. Samples were characterized using various instruments.

RESULTS:
The MNPs and OAMNPs were successfully synthesized (via co-precipitation method) and characterized by means of XRD, FTIR, TGA, FESEM, EDX, and TEM. OAMNPs and TAM were able to be encapsulated together inside PLGA (75:15). TAM was successfully loaded inside the PLGA and it was released by following a biphasic phase. The colloidal stability correlates well with the particle size

DISCUSSIONS:
MNPs and OAMNPs has a very small size which was less than 11 nm. OA coating managed to reduce the aggregation of the MNP. Their encapsulation was achieved by using O/W emulsion and evaporation technique. TAM-PLGA-OAMNPs size was about 132 nm obtained using TEM suitable for biomedical application.

CONCLUSION:
MNP can be used as an anti-cancer drug carrier because of its biocompatibility, ultrafine size, and its superparamagnetic nature. OAMNPs and TAM were able to be encapsulated together inside PLGA and TAM was successfully loaded inside the PLGA and it was released by following a biphasic phase.

REFERENCES:
1. Albert, Emmellie Laura, Yuki Shirosaki, and Che Azurahanim Che Abdullah. "Drug Release and Kinetic Study of Tamoxifen Citrate conjugated with Magnetite Nanoparticle for Drug Delivery Application." International Journal of Applied Engineering Research 13, no. 7 (2018): 5360-5369.

PARTICIPANTS ABSTRACT

CRM 05: Chemical and Green Synthesis of Gold Nanoparticles As Drug Delivery

Siti Nadiah Zulkifli[1], Manali Haniti Zahid[2], Iskandar Zulkarnain Alias[2], Che Azurahanim Che Abdullah[1], [1]Institute of Advanced Technology (ITMA), Universiti Putra Malaysia, 43400 Serdang, Selangor [2] Department of Chemical Pathology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

INTRODUCTION:
Gold nanoparticles (AuNPs) is chosen for this project due to the fact that it is widely used in a variety of biomedical application. This study investigate the advancement of nanotechnology focusing on nanomedicine to overcome current chemotherapeutic barriers in cancer treatment especially in diminishing the problems that are associated with traditional chemotherapy and multidrug resistance by focusing their unique nanoscale size and distinctive bioeffects of gold nanoparticles on colorectal cancer stem cells.

MATERIALS METHODS:
This research synthesis AuNPs by using chemical method and green synthesis. AuNPs were synthesis using the Turkevich method using HAuCl as precursor and trisodiumcitrate and plant extraction as reducing agent as well as stabilizing agent.

RESULTS:
After formation of AuNPs, characterization techniques like UV-Vis Spectroscopy, microscopy and some other detection methods were used to characterize and analyse the changes in sizes and shapes.

DISCUSSIONS:
One step green synthesis method can reduce metal ions to nanoparticles. It is due to the presence of biomolecules in plant extracts (Mittal et al., 2013). There are a few advantages using plant extract as a reducing agent which are involving one step synthesis, easy to prepare and environmental friendly (Kulkarni et al., 2014).

CONCLUSION:
Nanoparticles produced by plant extractions are more stable and the rate of green synthesis is faster compared to the chemical synthesis.

REFERENCES:
1. Mittal, A. K., Chisti, Y., & Banerjee, U. C. (2013). Synthesis of metallic nanoparticles using plant extracts. Biotechnology advances, 31(2), 346-356.
2. Kulkarni, N., & Muddapur, U. (2014). Biosynthesis of metal nanoparticles: a review. Journal of Nanotechnology, 2014.

CRM 06: Green Synthesis of Reduced Graphene Oxide and Cytotoxicity Studies

Dharshini Perumal[1], Mas Jaffri Masarudin[2], Ahmad Azmin Mohamad[3], and Che Azurahanim Che Abdullah[1]
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INTRODUCTION:
Nanomaterials are on the route to provide novel approach in cancer treatments. In the present study, simple, facile and bio-compatible green synthesis of reduced graphene oxide (rGO) using plant extract that act as a capping agent were used. Hence, it serves as a promising nanomaterial for application in cancer treatments.

MATERIALS METHODS:
Graphene oxide (GO) was prepared following the Improved Hummer's method[1]. For the synthesis of rGO, plant extracts were added to the GO suspension and stirred for 12 h. The synthesized rGO were characterized using various analytical techniques. The in-vitro analysis of cytotoxicity was carried out using rGO obtained against brine shrimp and A549 cancer cell lines.

RESULTS:
The reduction of GO was confirmed by the analytical techniques including UV-Vis, XRD, FT-IR, DLS, and Raman spectroscopy. The cytotoxicity assay was performed to assess the targeting capability and anticancer properties of prepared rGO. These rGO showed excellent biocompatibility on brine shrimp. Preliminary data shows significant cytotoxicity on cancer cell lines. In summary, environmentally friendly rGO prepared plays a vital role in the future nanomaterial-based cancer treatments.

DISCUSSIONS:
The green synthesis of rGO have been successfully prepared using plant extract and well characterized with UV–vis, XRD, FT-IR, DLS and Raman spectra. The rGO showed significant cytotoxic activity against cancer cell lines such as A549. Cytotoxicity tests of the prepared nanomaterial hypothesized to be dose dependent.

CONCLUSION:
Our results concluded that plant-derived rGO was successful and the future work will be on the incorporation of silver nanoparticles and rGO for potential synergistic effect, which may open a new avenue for cancer treatments.

REFERENCES:
Marcano, D. C., Kosynkin, D. V, Berlin, J. M., Sinitskii, A., Sun, Z., Slesarev, A., Alemany, L. B., Lu, W., Tour, J. M. (2010). Improved synthesis of graphene oxide. ACS Nano, 4(8), 4806–4814.

PARTICIPANTS ABSTRACT

CRM 07: The Use of Tumour Antigen Dna Vaccine in Combination with Anti-pd1 Improves Tumour Control in Transgenic Cancer Model

Kue Peng Lim[1], Nur Syafinaz Zainal[1], San Jiun Chai[1], Bryan Lye[1], Chai Phei Gan[1], Natasha Zulaziz[1], Chuan Wang[2], Ruhcha V Sutavani[2], Christian Ottensmeier[2], Emma King[2], Gareth Thomas[2], Natalia Savelyeva[2] & Sok Ching Cheong[1]

[1]Head and Neck Cancer Research Team, Cancer Research Malaysia, Malaysia, [2]Cancer Sciences, University of Southampton, UK

INTRODUCTION:

The use of checkpoint inhibitors has revolutionized cancer therapy. However, there is still a majority of patients do not respond to this type of treatment. Lack of inherent T cells infiltrating into the tumour is believed to be one of the major factors rendering checkpoint inhibitors ineffective. Cancer vaccines targeting specific tumour antigens work to elevate the levels of antigen-specific T cells. Hence combining checkpoint inhibitors with cancer vaccines is expected to improve patient outcomes. Here we present our work in evaluating a dual antigen cancer vaccine in combination with anti-PD1 in a transgenic murine model.

MATERIALS METHODS:

The B16F10 syngeneic cancer cell line was inoculated subcutaneously in the B6.Cg-Tg(HLA-A/H2-D)2Enge/J transgenic model. Day 3 post-inoculation, anti-PD1 was given every three days and two doses of DNA vaccine were given on day 5 and day 22. Animals were monitored for tumour growth and euthanized on day 35. Blood, spleen and tumour from vaccinated and non-vaccinated animals were used to examine the levels of immune cells using ELISPOT and flow cytometry assays.

RESULTS:

The use of DNA vaccine increased the infiltration of immune cells into the tumour and delayed the growth of tumour compared to control animals. Additionally, immune cells of DNA vaccinated animals have markedly upregulated the expression of checkpoint protein, PD1 as a consequence of immune activation. Its then rationalized the use of DNA vaccine in combination with anti-PD1 could further improve tumour control. Indeed, when DNA vaccine is used in combination with anti-PD1, complete tumour growth inhibition was observed.

DISCUSSIONS:

DNA vaccine successfully induced immune cells infiltration and subsequently tumour control. Further, the activation of immune responses also up-regulated checkpoint protein expression. This observation confirms that the implementation of immunotherapy involves increasing immune activation and reducing immune suppression is important.

CONCLUSION:

The combination of antigen-specific DNA vaccine with anti-PD1 is effective in controlling tumour growth.

PARTICIPANTS ABSTRACT

CRM 08: Feasibility and Psychosocial Impact of Mainstreaming Genetic Counselling for Genetic Testing of Brca1 and Brca2 in Ovarian Cancer Patients in Malaysia (Magic Study)

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INTRODUCTION:
Identification of germline BRCA mutations in ovarian cancer patients allows clinicians to take appropriate medical management and preventative measures for patients and their relatives. However, due to shortage of genetic counsellors and clinical geneticists, and lack of awareness among clinicians, there is inadequate genetic testing in most part of Asia. Mainstreaming genetic counselling may increase accessibility to genetic testing.

METHOD:
This study aimed to recruit 800 patients with non-mucinous epithelial ovarian, peritoneal or fallopian tube cancer regardless of age or family history. Patients are recruited either via mainstreaming (counselled by clinician) or traditional genetic pathway (referred to genetics service). Genetic Counselling Satisfaction Scale (GCSS), Decisional Conflict Scale (DCS), Psychosocial Aspect of Hereditary Cancer (PAHC) and Cancer Worry Scale (CWS) were used to measure the feasibility and psychosocial outcomes. Clinicians provided feedback on their experience with mainstreaming through a questionnaire.

RESULTS:
800 patients were recruited, 690 via mainstreaming and 110 via genetics route. Most were satisfied with their pre-test GC (mean: 23.9; SD: 2.7) and result disclosure (mean: 24.6; SD: 2.6) sessions. Most (86%) did not face difficulties in making decision for testing. Participants with no issues in at least 5 out of 6 PAHC domains increased from 46% at pre-test GC to 62% at result disclosure. 80% of clinician surveyed are keen to continue mainstreaming and integrate BRCA testing into their clinical practice.

DISCUSSION :
Interim results showed satisfaction in the services, low decisional conflict and acceptable psychosocial impact with few differences between mainstreaming and traditional genetics pathway. Most clinicians are keen to continue with the service.

CONCLUSION :

Mainstreaming cancer genetics may be possible to improve access to genetic counselling and testing in Malaysia.

REFERENCES :
Rahman, N. (2014) Mainstreaming genetic testing of cancer predisposition genes. Clinical Medicine 14(4):436-439

PARTICIPANTS ABSTRACT

CRM 09: Quantitative Analysis of ROS Generation by Bismuth Oxide Nanoparticles, Cisplatin and Baicalein-rich Fraction for Proton Beam Therapy

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INTRODUCTION:

The application of radiosensitizers in radiotherapy is widely explored to target the effect of ionizing radiation on cancer cells while lowering side effects onto normal cells. Reactive oxygen species (ROS) is an important factor in killing the malignant cells. Here, we investigated roles of bismuth oxide nanoparticles (BiONPs), cisplatin (Cis), and baicalein-rich fraction (BRF) as radiosensitizers that might influence the ROS induction and hence reduced the cancer cells survival for proton beam therapy.

MATERIALS METHODS:

Colon cancer cells, HCT 116, were treated with BiONPs, Cis and BRF individually, as well as BiONPs-Cis (BC), BiONPs-BRF (BB), and BiOPNPs-Cis-BRF (BCB) combinations. The cells were exposed to 3 and 6 Gy of 150 MeV proton beams and ROS generation were quantified.

RESULTS:

The ROS levels increased at both doses 3 and 6 Gy. Irradiation with the presence of Cis alone produced the highest amount of ROS, followed by radiation with BC combination and BiONPs alone. However, the ROS induced by BRF, BB and BCB treatments were lower than the control.

DISCUSSIONS:

Cis, a clinical drug, is expected to induce a high volume of ROS that could eliminate the cancer cells. Cis could increase the ROS level due to the suppression of SESN1 proteins.[1] The presence of BC causes lower ROS amount than Cis alone but higher than BiONPs alone, maybe due to the radical scavenging and pro-oxidant properties of bismuth nanoparticles.[2] In contrast, compounds obtained from plants had been shown to have antioxidant and radioprotective properties.[3] In this study, BRF might activate reduction-oxidation reaction in the cells, and increase oxidative stress tolerance level of the cells.[4]

CONCLUSION:

The production of ROS was enhanced in cancer treatment with the presence of BiONPs and/or Cis, suggesting the potentials of BiONPs alone and BC combinations as radiosensitizers for proton beam therapy.

REFERENCES:

1. Narita N, Ito Y, Takabayashi T, et al. Int J Hyperth. 2018;35(1):269-278.
2. Shakibaie M, Forootanfar H, Ameri A, Adeli-Sardou M, Jafari M, Rahimi HR. IET Nanobiotechnology. 2018;12(5):653-657.
3. Dinda B, Silsarma I, Dinda M, Rudrapaul P. J Ethnopharmacol. 2015;161:255-278.
4. Patwardhan R. PhD dissertation, Homi Bhabha National Institute. 2015.

PARTICIPANTS ABSTRACT

CRM 10: Synthesis and Characterization of Graphene Oxide Functionalized with Magnetic Nanoparticle via Simple Emulsion Method

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INTRODUCTION:

Graphene oxide(GO) is a versatile nanoparticles which has honeycomb carbon geometry, one-atom thickness, large surface area and numerous functional groups so, it can immobilize a large number of materials[1][2]. Iron oxide(IO) is a magnetic nanoparticles which can be maintain at specific place by applying magnetic field hence it can be use in drug delivery[3]. GO large surface to volume ratio combined with IO superparamagnetic properties yield an interesting nanocomposite material for biomedical application.

MATERIALS METHODS:

Current research focusing on the loading of IO onto GO via simple emulsion technique. Proper modification was conducted by varying the ratios of GO to IO at 1:1, to 1:3 to discover the best amount of IO suitable to be loaded on GO.

RESULTS:

Samples GO-IO(1:1), GO-IO(1:2), and GO-IO(1:3) were characterize using various equipments. XRD data showed that all samples have diffraction peaks at (220), (311), (400), (422), (511), and (440) belonging to Fe_3O_4 which confirm the loading of IO to GO. Samples GO-IO(1:2) has the highest content of IO which is about 57% as exhibited in TGA. Besides that, VSM result indicated that the magnetic saturation of GO-IO(1:2) is 50emu/g which is the higher compare to other samples.

DISCUSSIONS:

XRD data confirmed that after IO loaded on GO, the GO main peak disappears indicating the prevention of GO stacking due to IO. Additionally, the magnetic saturation for GO-IO(1:2) is the highest among other GO-IO nano-composite because it has the most IO content as supported by TGA result.

CONCLUSION:

It is revealed that IO were successfully conjugated on GO with maximum magnetic saturation measured at the ratio of GO to IO of 1:2.

REFERENCES:

1. Rostamizadeh S. et al., Nanochem Res, 2017; 2, 1, 29-41.
2. Liu J. et al., Acta Biomater, 2013; 9, 12,9243-9257.
3. McBain, S. C. et al., Int J Nanomedicine, 2008; 3,169-180.

PARTICIPANTS ABSTRACT

CRM 11: Germline BRCA1 and BRCA2 Variants in Malaysian Ovarian Cancer Patients

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INTRODUCTION:

BRCA1 or BRCA2 (collectively BRCA1/2 hereafter) pathogenic variant detection may identify a subset of ovarian cancer patients that may benefit from platinum derivatives and poly (ADP-ribose) polymerase inhibitors. BRCA1/2 frequencies in ovarian cancer patients range from 15 20%, varying across ethnic populations [1]. Limited population based cohorts exist for Asians, with the exception of Chinese [2]. This will be the first multi ethnic Malaysian ovarian cancer population cohort.

MATERIALS METHODS:

Women with non mucinous epithelial ovarian, peritoneal or fallopian tube cancer were prospectively recruited to the MaGiC Study from August 2016 to October 2019. Germline DNA was subjected to Hi Plex next generation sequencing method [3] and multiplex ligation dependent probe amplification to detect single nucleotide variants, small insertions/deletions and exon deletions/duplications in the BRCA1/2 genes.

RESULTS:

Results from 790 patients tested until September 2019 have identified BRCA1 or BRCA2 pathogenic/likely pathogenic variants in 9.2% and 4.7% patients, respectively. Variants of uncertain significance were detected in 11.4% patients and no pathogenic variants were detected in 74.7% patients. 44% (4/9) of patients with breast and ovarian cancers had a BRCA1/2 pathogenic variant. Among BRCA1/2 carriers with complete clinical and epidemiological data, 84% (68/81) did not have a typical family history of BRCA1/2 related cancers. The most common histotype for BRCA1/2 carriers was high grade serous ovarian carcinoma (50/81).

DISCUSSIONS:

Our study provides the frequency and spectrum of BRCA1/2 variants in ovarian cancer unselected for age and family history. The higher number of BRCA1 pathogenic variants, common high grade serous histotype and incidence of both breast and ovarian cancers among BRCA1/2 carriers are in accordance with previous studies [4].

CONCLUSION:

Prevalence data from this study signifies a need for greater patient access to BRCA1/2 testing and efficient referral of carriers to limited genetic services in Malaysia.

REFERENCES:

[1] Shanmughapriya S et al. Oncology 2013; 84(4): 226-32.
[2] Li A et al. Gynecol Oncol 2018; 151(1): 145-152.
[3] Hasmad HN et al. Gynecologic Oncology 2016; 141(2): 318-322.
[4] Cardoso FC et al. Hum Genomics 2018; 12(1): 39.

CRM 12: Baseline SUV Determination from the Normal Spine of Breast Cancer Patients using Semi-Quantitative 99mTC-MDP SPECT/CT

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INTRODUCTION:
The integration of computed tomography (CT) into single-photon emission computed tomography (SPECT) has managed to improve the diagnostic practice of Nuclear Medicine physicians by enabling semi-quantitative assessment of radiotracer uptake using standard uptake value (SUV) parameter. However, the number of literatures is still low. Thus, the aim of this work is to determine the SUV of 99mTC-MDP radiotracer from the normal spine of breast cancer patients using a SPECT/CT system, to serve as a baseline for differentiating normal and metastatic bone.

MATERIALS & METHODS:
Skeletal SPECT/CT of 30 female breast cancer patients were retrospectively acquired. The mean SUVs (SUVmean) and maximum SUVs (SUVmax) from the normal spinal structures (thoracic and lumbar regions) were generated using the Q.Metrix™ software. The data were then categorised and compared based on the body weight (BW) and body surface area (BSA) calculations.

RESULTS:
A total of 286 normal spinal structures were identified from the SPECT/CT images. The calculated SUVs have low values but possess wide variability. The mean ± standard deviation of SUVmean and SUVmax were presented as follows: BW = 3.90 ± 1.60 and 6.50 ± 2.80; BSA = 1.05 ± 0.40 and 1.80 ± 0.70. The mean coefficient of variation (CoV) for SUVmean were found to be slightly lower than SUVmax. No significant differences in CoV were observed for SUVmean and SUVmax during BW and BSA calculations.

DISCUSSIONS & CONCLUSIONS:
According to the investigational conditions, the 99mTC-MDP SUV for normal spine were able to be quantified and consistent with previous reports. Metastatic bone in breast cancer patients were expected to show higher uptake due to the greater osteoblastic activity. A larger pool of data is warranted to further confirm these findings, before full utilisation in the clinical settings can be achieved.

REFERENCES:
1. Ross JC et. al. European J Hybrid Imaging 2019; 3: 8
2. Kaneta T et al. Am J Nucl Med Mol Imaging 2016; 6(5): 262-268.

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