STEM CELL &
CANCER SYMPOSIUM
SCCS 2018

UNIVERSITI MALAYA | FACULTY OF MEDICINE

ABSTRACT BOOK

"Exploring New Horizons in Cancer & Stem Cell Research"

STEM CELL & CANCER SYMPOSIUM 2018

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FOREWORD

Greetings from SCCS 2018!

It gives me great pleasure to welcome you all to the Stem Cell and Cancer Symposium (SCCS) 2018 held on the 17-18th October 2018 at Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia. This is our very first meeting amalgamating the two key research niches; Stem Cell and Cancer, hence the theme "Exploring New Horizons in Cancer and Stem Cell Research" illuminates it well.

In the era of rapid progress in understanding stem cell and cancer biology, it is intriguing to know the molecular, cellular and systemic regulation are very similar in stem cell and cancer to a degree, but they have very different impact on health. Hence, a dynamic interaction between researchers from both fields would enable better understanding the mechanism by which stem cell and cancer cells impact the homeostasis of cell, tissue and organs functions. Having said this, this symposium envisaged to be a tangible platform to explore the emerging field of cancer stem cell biology which is associated with tumour heterogeneity, self-renewal/tumour-initiation and drug resistance. It provided a perfect opportunity for scientific communities from clinic, academia and industry to gather for an insightful exchange of latest, innovative and cutting-edge research updates in the field of stem cell and cancer research to ensure your attendance worthwhile.

This 2-days meeting empowered the sharing of latest research findings not only by world-renowned experts but also our researchers through oral and poster presentations, thought-provoking "Junk the Jargon: Stem*CER* in 180 seconds!" talent showcase. As an avenue to move forward in these fields, a cancer forum by experts brought leading researchers, clinicians and entrepreneurs together to address some of the key challenges and evolving solutions to break the barriers within and between the fields of stem cell and cancer. Not to miss, the Stem Cell Debate by experts in the field will not only be a steering and fruitful dialogue, it was a fun and enlightening interactive session! I encourage readers of conference abstract book to take this opportunity to learn key findings and research progress in the field of stem cells and Cancer Biology.

My deepest appreciation goes to all the speakers and panellists. On behalf of organising committee and faculty, I would like to extend our warm welcome to colleagues from Taipei Medical University, Taiwan for your support to this meeting. Heartfelt thanks to Journal of Health and Translational Medicine (JUMMEC) for the tremendous support.

Thank you.

DR. THAMIL SELVEE RAMASAMY
Chair
Stem Cell & Cancer Symposium (SCCS) 2018

JOURNAL OF HEALTH AND TRANSLATION MEDICINE (formerly known as Journal of the University Malaya Medical Centre)
JUMMEC

LIST OF ABSTRACTS FOR ORAL PRESENTATION

ORAL-01

CONDITIONED MEDIUM FROM M1 MACROPHAGE, BUT NOT M2 PHENOTYPE INDUCE TUMOUR SUPPRESSION OF THE CT26 AND 4T1 CELL LINES

Noorzaileen Eileena Zaidi[1], Nor Aini Lubis Mhd Zain[1], Nur Aima Hafiza Shazali[1], Mohd Azuraidi Osman[1], Leow Thean Chor[1], Kamariah Ibrahim[3], Nik Mohd Afizan NAR[1,2,*]

[1]Department of Cell and Molecular Biology, Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.
[2]Institute of Tropical Forestry and Forestry Products (INTROP), Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.
[3]Department of Biomedical Science, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.

Introduction
Contradicting studies have shown that tumour-associated macrophages infiltrated in colorectal cancer and breast cancer could either result tumour progressing or tumour repressing characteristics. In basis of the study, we sought to determine the effects of conditioned medium from macrophages, significantly the classically activated macrophages, on the cellular growth of the cancer cells, which is believed to mediate tumour proliferation/apoptosis.

Methodology
Murine (CT26 and 4T1; colorectal cancer and breast cancer) cell lines were exposed with conditioned medium (CM) from lipopolysaccharide (LPS) and interferon gamma (IFNγ) that was used as an inducer of M1 macrophage differentiation, meanwhile interleukin-4 (IL-4) and IL-13 to differentiate macrophage to M2 phenotype. Both CM were generated during differentiation (M1diff; M2diff) and after differentiation (M1; M2). Viability studies were performed using MTT assay, annexin V-FITC assay including cytokine profile were quantified using real time qPCR.

Results
M1diff and M1 CM resulted in 50% apoptosis of CT26 and 4T1 cells, but not the M2diff and M2 CM, which resulted in proliferation of these cancer cells. Among the cytokines released by M1 macrophages, tumour necrosis factor α (TNFα), IL-12 and nitric oxide (NO) production were examined by direct addition to CT26 and 4T1, but neither mediates tumour proliferation. M2diff and M2 CM resulted in secretion of IL-10, anti-inflammatory cytokine.

Discussion
We identified CM of M1 phenotype macrophage attenuated the tumoricidal activity in the CT26 and 4T1 cells that disseminates the growth of colon and breast cancer cells, but not by the M2 phenotype of macrophages. It is clear that cytokines secreted by M1 macrophage play an active role in promoting the tumour cells to induce apoptosis signalling and suppressed tumour growth.

Conclusion / Summary
Our results indicate that M1 macrophage exerts tumoricidal activity on colon and breast cancer cells by secreting cytokines and have the potential to contribute anti-tumour effects in *vivo*.

Keywords
M1 macrophage, M2 macrophage, Tumoricidal, CT26, 4T1

ORAL-02

PRO-ONCOGENIC PROTEIN AGR2 CONTROLS EPCAM EXPRESSION AND RECEPTOR PRESENTATION TO THE CELL SURFACE

M. Aiman Mohtar[1,2*], Rory Duncan[3], Borek Vojtesek[4], Ted R Hupp[2,4]

[*1] UKM Medical Molecular Biology Institute (UMBI),The National University of Malaysia, Cheras, 56000 Kuala Lumpur, Malaysia
[2] Institute of Genetics and Molecular Medicine, University of Edinburgh, EH4 2XR, Edinburgh, United Kingdom
[3] Institute of Biological Chemistry, Biophysics and Bioengineering, Heriot-Watt University, EH14 4AS, Edinburgh, United Kingdom
[4] Regional Centre for Applied Molecular Oncology, Masaryk Memorial Cancer Institute, 656 53 Brno, Czech Republic

Introduction

Anterior gradient-2 (AGR2) is a pro-oncogenic protein that belongs to a protein disulfide isomerase superfamily. It is mainly overexpressed in diverse types of cancer and its elevated expression predicts poor prognosis in cancer patients. Mechanism of how AGR2 function in cancer emergence is poorly understood. Recently, we showed that AGR2 protein has a unique property that it can bind sequence specifically to a TxIYY peptide-docking motif present in client proteins such as epithelial adhesion molecule (EpCAM).

Methodology/Results

Here, we showed using immunohistochemistry that AGR2 and EpCAM are highly expressed in 90% of esophageal adenocarcinoma tissue microarray cores (n=91) including lymph node metastases. AGR2 and EpCAM showed significant positive relationship ($p<0.0001$) suggesting that the two molecules are highly co-expressed in esophageal adenocarcinomas. Proximity ligation assays demonstrated that endogenous AGR2 and EpCAM form protein-protein complexes in cancer cells which is consistent with co-localization of ectopically expressed and fluorescently tagged proteins observed using confocal and wide field fluorescent microscopy. Cell-based systems were then developed to further understand the dynamics of AGR2:EpCAM interaction by reconstituting their expression in FLO-1 esophageal cancer cell line. The transfection of CHERRY- AGR2 can stimulate the production of GFP-EPCAM protein in cells as defined by both western blotting and wide-field fluorescent microscopy. Interestingly, the presence of AGR2 in the endoplasmic reticulum is required for EpCAM receptor delivery to the plasma membrane.

Discussion

Results thus far suggest that AGR2 act as a regulator of EpCAM signaling by promoting receptor presentation from the endoplasmic reticulum to the cell surface. High co- expression of AGR2 and EpCAM in esophageal adenocarcinomas suggest that both proteins may serve as physiologically relevant candidates for cancer biomarker and future therapeutic intervention.

Conclusion / Summary

Our data provide the role for the sequence-specific docking of an ER-resident chaperone protein and present one mechanism for controlling EpCAM-mediated signaling and highlights a potential ‘’druggable’’ stage in the oncogenic secretory pathway.

Keywords

protein disulfide isomerase, secretory pathway, peptide motif, oncogene, endoplasmic reticulum

ORAL-03

EVALUATING ANTIPROLIFERATIVE ACTIVITIES OF HYBRIDIZED PEPTIDES AGAINST HEPATOCELLULAR CARCINOMA CELLS (HEPG2)

Chu Xin Ng[1], Cheng Foh Le[2], Sau Har Lee[1,*]

[*1]School of Biosciences, Faculty of Health and Medical Sciences, Taylor's University, Lakeside Campus, Subang Jaya, Selangor, Malaysia
[2]School of Biosciences, Faculty of Science, University of Nottingham Malaysia Campus, Selangor, Malaysia.

Introduction
Short peptides have acquired increasing interest as promising therapeutics, particularly as anti-cancer alternatives during the recent years. They have been reported to demonstrate incredible anti-cancer potentials through targeting signalling transduction pathways, as well as modulation of cell cycle, tumour suppressor proteins and transcription factor. Peptides are primarily of interest due to its rapid kinetics, high potency, and low biocompatibility issue. In search of novel anticancer leads, the main objective of this study is to evaluate the *in-vitro* antiproliferative properties of five hybridized peptide analogues against human hepatocellular carcinoma (HepG2) cell line.

Methodology
Five DN analogues (DNs) were designed based on two parent peptides, NDC1 and NDC2, through fragments hybridization approach. Modification of amino acid residues at specific positions of NDC1 and NDC2 was done at the C-terminal. Then, MTT assay was performed to examine the antiproliferative activities of NDC1, NDC2 and DNs against HepG2 cells at concentrations ranging from 2-256µg/mL for 24 hours.

Results
The parent peptide, NDC1 showed an IC50 value of 87±2.404µg/mL at 24 hours while NDC2 did not display antiproliferative activity against HepG2 cells. Among the DNs, DN4 was found to exhibit positive antiproliferative activity against HepG2 cells, with IC50 value 168±34.33µg/mL. In contrast, DN3 showed minimal antiproliferative activity with IC50 value >256µg/mL. DN1, DN2 and DN5 did not demonstrate any antiproliferative activity against HepG2 cells.

Discussion
Replacement of lysine and leucine in NDC1 to valine and aspartic in DNs might have attributed to the decreased antiproliferative activity. Besides, further diminished activity in DN3 in contrast with DN4 is due to the methyl end branching at the aliphatic functional group. The absence of activity in DN1 and DN2 might also be caused by the substitution of glycine to lysine. Introduction of arginine into the peptide sequence most possibly led to the loss of DN5 cytotoxicity against HepG2 cells.

Conclusion
Modified DNs possessed diminished to negative antiproliferative activities against HepG2 cells. Hence, the amino acid sequence of DNs should be further studied to develop a potent anti-cancer therapeutic drug.

Keywords:
Anticancer peptides, liver cancer, chemotherapy, multidrug resistance, peptide fragments hybridization.

ORAL-04

KNOCKDOWN OF TOUSLED-LIKE KINASE 1 INHIBITS GLIOBLASTOMA CELL INVASION AND MIGRATION VIA THE INTEGRIN-MEDIATED CELL ADHESION PATHWAY

Kamariah Ibrahim[1,2*], Nor Azian Abdul Murad[1], Roslan Harun[3] and Rahman Jamal[1]

[1]UKM Medical Molecular Biology Institute, National University of Malaysia, 56000, Kuala Lumpur
[*2]Department of Biomedical Science, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia
[3]KPJ Ampang Puteri Specialist Hospital, 1, Jalan Mamanda 9, Taman Dato Ahmad Razali, 68000 Ampang, Selangor

Introduction
GBM cells have the ability to aggressively infiltrate or invade into the normal brain tissues and along the vascular tracks, which hinders complete resection of all malignant cells. Therefore, gaining a deeper understanding of GBM invasive phenotypes is crucial in hoping that the gained knowledge would lead to novel GBM treatments that are more effective and less toxic. Tousled-like kinase 1 (TLK1), a serine/threonine kinase was found to be a potential target for GBM. In this study, functional role of TLK1 in GBM cancer invasion and migration were investigated.

Methodology
TLK1 knockdown in GBM cells namely U87MG and LN18 were performed using siRNA and shRNA. Invasion and migration capabilities of these knockdown GBM cells were assessed using trans-well invasion and migration assays, wound healing assay and cell adhesion array. Downstream pathways investigation involved utilization of functional gene expression microarray and q-PCR. ELISA based Total/phosphorylated TP53, Erk/AKT/p70 S6K and GTP-bound levels of RAC and CDC42 activation assay was performed to validate TLK1 downstream pathways.

Results
Knockdown of TLK1 significantly inhibited invasion and migration of both U87MG and LN18 cells as well as wound healing. Morphological changes were observed suggesting inhibition of lamellipodia, filopodia of GBM cells. Knockdown of TLK1 however, showed significant increase in cell adhesion towards laminin. Microarray analysis showed involvement of integrin-mediated cell adhesion pathway. Protein analysis confirmed that TLK1 knockdown resulted in inhibition of p70S6K, as well as components of Rho-GTPase and integrin-mediated cell adhesion pathway components; RAC2 and CDC-42 in U87MG.

Discussion
TLK1 was only found to be involved in DNA replication, mitosis and cytokinesis. Emerging studies reported that TLK1 have important role in the regulation of cellular motility. Our finding supported the critical function of TLK1 in promoting GBM invasiveness.

Conclusion / Summary
These results suggest novel role of TLK1 in GBM cancer invasion and migration through integrin-mediated of RAC2-CDC42-PAK2 pathway.

Keywords
Glioblastoma – TLK1 – invasion and migration – integrin pathway

ORAL-05

KNOWLEDGE, AWARENESS AND PERCEPTION OF PREGNANT WOMEN IN KUALA LUMPUR ON CORD BLOOD STEM CELLS BANKING

Vinodhini Bhaskaran[1], Farahnaz Amini[1]

[1] School of Healthy Aging, Medical Aesthetics, Regenerative Medicine, Faculty of Medicine and Health Sciences, UCSI University

Introduction
Umbilical cord blood (UCB) is an alternative and non-invasive source of hematopoietic stem cells. However, the lack of knowledge and awareness about UCB banking is a global problem. This study was aimed at assessing awareness, knowledge and perception of UCB banking in Malaysian pregnant women.

Methodology
A survey was done using a questionnaire with a total of 39 questions, of which 16 questions measured the level of knowledge. Every correct answer was given 1 point, expecting the total score to range from 0 to 16. Educational brochures were distributed among participants. Recruitment was done in antenatal clinics and hospitals in Kuala Lumpur in accordance with the set inclusion and exclusion criteria following ethics approval.

Results
A total of 255 pregnant women aged 18 to 50 years participated in this survey. Majority of them were Indian, first time mothers and 25 to 35 years old. About 44.4% had a Diploma, 24.3% a Bachelor degree with about 34.3% from medical field. The mean score of awareness and knowledge was 3.00 ± 2.15 and 4.86 ± 4.01 respectively. The higher age was associated with greater knowledge ($p= 0.002$) and having more children was significantly associated with both higher level of awareness ($p=0.018$) and greater knowledge ($p=0.032$). A non-significant difference was observed between level of awareness and educational background. Monthly family income was significantly associated with both higher level of awareness ($p= 0.006$) and knowledge ($p=0.006$). Only one third of the participants were aware of UCB banking with only 7.9% having good knowledge levels. The majority of participants had acquired their knowledge through media and friends with only 31.5% from their health care providers.

Discussion
Unlike western countries, in Malaysia, most of the information received by public on UCB banking is from private UCB banks. Educating public and especially pregnant women, may help them to make an informed choice regarding banking or donating their baby's UCB.

Conclusion / Summary
Pregnant women in this study have poor level of awareness and knowledge about UCB banking. Knowledge and awareness seemed to have a direct effect on the perception of participants and reflected in their choice of UCB banking and donation.

Keywords
Awareness; Cord blood stem cells banking; Knowledge; Perception; Pregnant women

ORAL-06

AWARENESS, KNOWLEDGE, ATTITUDE AND PERCEPTION ON STEM CELLS AMONG RESIDENTS IN KLANG - A PILOT STUDY

Balachandran M. [1], Tan Chung Keat[1], Eugenie Tan Sin Sing[1], Farahnaz Amini[1], Marjan Sadat Seghayat[1], Normina Ahmad Bustami[1], Sharmanee Thiagarajah[1]*

[1] School of Healthy Aging, Medical Aesthetics and Regenerative Medicine, Faculty of Medicine and Health Science, UCSI University, 56000, Kuala Lumpur, Malaysia.

Introduction
Stem cell (SC) research and treatment is fast gathering interest and promises cure for many diseases. Public awareness on stem cells is largely understudied and reports are scanty. As such, this study aims to (a) asses awareness, knowledge, attitude and perception of Klang residents on SC and (b) assess associations between socio-demographic factors with levels of awareness and knowledge on SC.

Methodology
Consenting, Malaysian citizens aged 20 and above who were able to read and write in English.One hundred and twenty-five participants were recruited in a cross sectional study upon informed consent. They were subjected to a questionnaire consisting of five domains; namely socio-demographics as well as awareness, knowledge, attitude and perception on SC. Scores for awareness were assigned with 10-16 as high, 6-10 as moderate and 0-5 as low level. Scores for knowledge with 5-6 as high, 3-4 as moderate and 0-2 as low level scoring. Data analysis were analysed descriptively and associated using Chi-square cross tabulation. Statistical significance were accepted at $p<0.05$ (significant) and $p<0.01$ (very significant).

Results
Most participants were female (67.2%), age group of 20-29 (51.2%), Malays (54.4%), married (52%), total household income more than RM 5000 (39.2%) and had tertiary education (71.2%). In awareness, 16% of participants had high while 34% had moderate scoring. In levels of knowledge, 23% scored high and 35% scored moderate. SC awareness and knowledge levels were significantly associated with household income ($p<0.05$) and participant's occupation ($p<0.05$). Awareness and education levels were significantly associated with unproven SC treatments such as in aesthetics and chronic diseases ($p<0.01$). Willingness to pay for SC treatments were very significantly associated with awareness ($p<0.01$), levels of knowledge ($p<0.01$), attitude ($p<0.01$), and household income ($p<0.01$). Meanwhile, perception was significantly associated with religion and cultural background ($p<0.05$).

Conclusion
Results on this study reported mediocre level of awareness and knowledge among residents in Klang on SC. Awareness, knowledge, attitude and perception of SC were significantly associated with level of education, household income, occupation, willingness to pay, religion and cultural background. Concerted efforts to increase public awareness and knowledge are necessary and larger scale study may warrant more comprehensive overview.

Keywords
stem cell, awareness, knowledge, perception, attitude

ORAL-07

CIRCULAR RNA-EPHB4 AS A PROMISING BIOTARGET IN COLORECTAL CANCER

[1]Nadiah Abu, [1]Siti Nurmi Nasir, [1]Sazuita Saidin, [1]Muhiddin Ishak, [2]Luqman Mazlan, [3]Isa Mohamad Rose, [1]Nurul Syakima Ab Mutalib and [1]Rahman Jamal

[1] UKM Medical Molecular Biology Institute (UMBI), Kuala Lumpur, Malaysia
[2] Department of Surgery, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
[3] Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Introduction
Circular RNAs are a class of non-coding RNAs that have been reported to be aberrantly expressed in diseases such as cancer and other neurodegenerative diseases. In fact, circular RNAs were found to be important regulators in the cellular machinery. In colorectal cancer (CRC), it has been discovered that there are a certain number of circular RNAs that are dysregulated. Among the differentially expressed circular RNAs, circ-EPHB4 was found to be a promising target. Therefore, this study is aimed at understanding the role of EPHB4, particularly in CRC.

Methodology
The circRNA-EPHB4-miRNA-mRNA prediction was performed using the Circinteractome, Targetscan and MirDB databases. The pathway and GO analysis was then performed for the identified genes using the ToppFun software. The expressions of both circ-EPHB4 and linear EPHB4 were detected in CRC cell lines and CRC tissues. The functional role of both circ-EPHB4 and linear EPHB4 were also validated *in vitro* via cell adhesion, wound healing, cell cycle and drug sensitivity assays.

Results
Circ-EPHB4 was predicted to bind to 4 miRNAs, namely miR-1182, miR-1298, miR-767-3p and miR-1248. Based on the target prediction, the genes associated with these miRNAs were found to be enriched in the FoxO signaling pathway as well as in the adhesion-related bioactivity. The expression of both circ-EPHB4 and linear-EPHB4 were found to be higher in CRC cell lines than the non-cancerous cell lines. A similar pattern was also observed in the clinical tissues. By targeting the linear EPHB4 and circEPHB4, the migration abilities, the cell cycle and the resistance of colorectal cancer cells towards 5-fluorouracil and Oxaliplatin were reduced. Besides that, silencing the circEPHB4 also affected adhesion to several extracellular matrix proteins such as laminin, fibronectin, collagen I and collagen IV.

Conclusion
The roles of circ-EPHB4 in CRC was elucidated for the first time. Collectively, the present study indicates that circ-EPHB4 can be a promising target to understand the molecular mechanism of CRC.

Keywords
circular RNA, CRC, EPHB4

ORAL-08

THE PROGNOSTIC ROLE OF TUMOR ASSOCIATED MAST CELLS IN ORAL SQUAMOUS CELL CARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Anand Ramanathan[1,2,*], Shaju Jacob Pulikkotil[3,], Gou Rean Wong[2], Lalli Dharmarajan[4], Zuraiza binti Mohd Zaini[1,2]

[*1] Department of Oral & Maxillofacial Clinical Sciences, Faculty of Dentistry, University of Malaya, 50603 Kuala Lumpur, Malaysia.
[2] Oral Cancer Research and Coordinating Centre, Faculty of Dentistry, University of Malaya, 50603 Kuala Lumpur, Malaysia.
[3] Division of Clinical Dentistry, School of Dentistry, International Medical University, Kuala Lumpur, Malaysia.
[4] School of Postgraduate Studies and Research, Masters in Molecular Medicine, International Medical University, Kuala Lumpur, Malaysia.

Introduction
The presence of mast cells (MC) in the tumor microenvironment is controversial with poor prognosis in other tumours (e.g. Hodgkin's lymphoma, malignant melanoma, squamous cell carcinoma (SCC) of oesophagus, lung and gastrointestinal adenocarcinoma) whereas good prognosis seen is some cancers (e.g. prostate, colorectal and clear-cell renal cell carcinoma). This systematic review and meta-analysis investigated the prognostic value of mast cells in oral SCC.

Methodology
In this systematic review, Ovid, Pubmed, Science Direct, Scopus and Web of Science were searched for publications that investigated the prognostic value of mast cells in OSCC. A meta-analysis was performed to calculate the pooled hazard ratio (HR) from data on the association between mast cell count (high versus low counts) and overall survival (OS), recurrence and lymph node metastasis.

Results
The number of studies included for systematic review was 11 and those included in meta-analysis for OS, lymph node metastasis and recurrence were two each. A pooled analysis indicated no significant prognostic role for mast cells (HR 0.71 (95%CI 0.322–1.58) (p-value = 0.121) for lymph node metastasis, (HR 0.44 (95%CI 0.02–10.00) (p-value = 0.036) for recurrence, and (HR 0.69 (95%CI 0.05–1.34) (p-value = 0.081) for OS in OSCC.

Discussion
The presentation will discuss the limitation of this study and the prognostic role of the mast cell in OSCC.

Conclusion / Summary
This study does show that there is no prognostic role of mast cells for lymph node metastasis, recurrence, and OS in OSCC. However, there were only a few studies, which could be included in this study. Therefore, further studies with more sample size, specific tumour sub-sites, stage, and treatment are required to provide an in-depth insight into the prognostic role of mast cells in OSCC.

Keywords
Mast Cell, Oral Squamous Cell Carcinoma, Prognosis, Overall Survival, Recurrence

ORAL-09

MORPHOLOGICAL CHANGES OF STEM CELL CYTOSKELETONS AFTER OXIDANT DAMAGE BY HYDROGEN PEROXIDE AND OTHERS

Nurul Kabir*, Suhaimi Draman and Durriyyah Sharifah Hasan Adli

Institute of Biological Sciences, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction

Many diseases affecting human life quality, such as Alzheimer's disease, diabetes or heart diseases show pathological disturbances of tissue regeneration. Because of their unique regenerative abilities, stem cells offer new potentials for treating such diseases. The microtubules and F-actin cytoskeleton of the neuronal cells undergo severe changes and develop intracellular aggregations such as neurofibrillary tangles composed of the microtubule binding protein Tau after oxidant damage and cause neuronal cell death. This study investigated the roles of microtubule and actin cytoskeleton of the stem cells in the pathogenesis of neurodegenerative or other disorders involving the death of stem cells.

Methodology

Rat bone marrow **M**esenchymal **S**tem **C**ells (MSCs) were isolated from the femur of *Sprague Dawley* and was cultured in Dulbecco's Modified Eagle's Medium (DMEM) media. They were treated with different concentrations of hydrogen peroxide (H2O2) or cytotoxic agents such as thymoquinone, thymol or carvacrol to produce oxidant damage to the stem cells. Triple-label immunocytochemistry was performed post-treatment to observe the nucleus, F-actin and microtubules of each affected cells using DAPI, Alexa488-labeled phalloidin and Cy3-labeled anti-tubulin antibody, respectively. Triple-channel high-resolution fluorescence microscopy pictures along with phase contract pictures were taken with a fluorescence microscope. The control and treated stem cell cytoskeletons were compared for differences.

Results

In the control, the stem cell cytoskeleton showed various morphologies most likely because of their pluripotent nature. F-actin was observed in stress fibers or as lamellapodia and filopodia. The microtubules showed regular arrangements which were spread out around a lightly stained nucleus. These arrangements of the F-actin and microtubules were severely disrupted after oxidant injury with H2O2 which also showed nuclear changes. The cytotoxic agents also disrupted the cytoskeleton in various ways.

Discussion

This study demonstrated the cytoskeletal changes occurring after oxidant damage to MSCs by H2O2 or other cytotoxic agents. The cells showed morphological changes which correlated with the changes observed in the F-actin, microtubules and the nucleus.

Conclusion / Summary

Oxidant damage could disrupt the cytoskeleton of the MSCs which correlate with the general morphological changes observed in the cells during cell death.

Keywords

Stem cell, microtubule, F-actin, oxidant damage

ORAL-10

CHARACTERISATION OF NOVEL ANTI-ANGIOGENIC COMPOUNDS FROM THE MALAYSIAN BIODIVERSITY

Mei Fong Ng[1], Kazuhide Shaun Okuda[1,3], Denver Desmond Britto[2], Norazwana Samat[1], Dedrick Song[1], Benjamin Hogan[3], Jonathan Astin[2], Pei Jean Tan[1] and Vyomesh Patel[1]*

[1] Drug Discovery Programme, Cancer Research Malaysia;
[2] School of Medical Sciences, University of Auckland, New Zealand;
[3] Institute of Molecular Biosciences, University of Queensland, Australia

Introduction
Tumour-associated angiogenesis plays a key role in tumour growth and cancer metastasis and thus, several anti-angiogenic drugs had been clinically approved as cancer therapeutics. However, majority of anti-angiogenic drugs are inhibitors of the VEGF-A/VEGFR-2 pathway, which showed inconsistent efficacy due to side effects and development of resistance.

Methodology
In Cancer Research Malaysia, we have utilized the *Tg(friend leukaemia integration 1 a (fli1a):EGFP)*^{y1} and *Tg(fli1:nEGFP)*^{y7} zebrafish transgenic line that has fluorescent blood vessels, to search for anti-angiogenic compounds from Malaysian natural products. With the observation in zebrafish, we then further investigated the underlying mechanism using Human Umbilical Vein Cells (HUVECs) by carrying out experiments such as cell proliferation assay and western blot. We have established a tumour-associated angiogenesis model using zebrafish and tested the compound using the model.

Results and Discussion
From our screen, we identified an alkaloid, C61 that inhibits zebrafish intersegmental vessel (ISV) and sub-intestinal vessel development at a concentration of 20 µM. Careful characterisation of *Tg(fli1:nEGFP)*^{y7} treated with C61 revealed that the endothelial cell number within the ISV was significantly reduced when compared to embryos treated with vehicle control. We observed that C61 treatment inhibited proliferation HUVECs via Click-iT proliferation assay in a dose dependent manner over 24 h treatment. As the VEGF-A/VEGFR-2 pathway is the most common pathway involved in angiogenesis, we investigated if C61 inhibits VEGFA-induced phosphorylation of VEGFR-2, and downstream targets includes ERK1/2, AKT and S6. Of note, C61 does not inhibit VEGF-A-induced phosphorylation of VEGFR-2, and its downstream targets ERK1/2, AKT and S6, indicating that C61 inhibits angiogenesis independently of the VEGF-A/VEGFR-2 pathway. Importantly, C61 is able to inhibit tumour-associated angiogenesis in a zebrafish B16F10 melanoma cell xenograft model, highlighting its relevance in targeting pathological angiogenesis.

Conclusion / Summary
In summary, we show that C61 exhibits anti-angiogenic properties in both developmental and pathological contexts in zebrafish independently of VEGF-A/VEGFR-2 pathway and may hold promise as a novel anti-angiogenic drug.

Keywords
Tumour-associated angiogenesis; zebrafish; natural product; VEGF-A/VEGFR-2 independent

ORAL-11

CHARACTERISATION AND EFFECT OF SECRETOME OF STEM CELLS FROM HUMAN EXFOLIATED DECIDUOUS TEETH ON THE PROLIFERATION OF CHONDROCYTES

Suleiman Alhaji Muhammad[1,], Norshariza Nordin[2], Paisal Hussin[3], Muhammad Zulfadli Mehat[4], Nor Hayaty Abu Kasim[5] and *Sharida Fakurazi[1,4]

[1]Institute of Bioscience, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[2]Department of Biomedical Science, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[3]Department of Orthopaedics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[4]Department of Human Anatomy, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[5]Department of Restorative Dentistry, Faculty of Dentistry, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction
Stem cells from human exfoliated deciduous teeth (SHED) represent postnatal stem cell population with high proliferative, self-renewal and multi-lineage differentiation capacity. Studies have shown that therapeutic benefit of stem cells is attributed to multiple secreted factors that modulate tissue microenvironment to evoke regeneration. The present study aimed to prepare secretome from SHED and characterise SHED cultured under different conditions.

Methodology
SHED were cultured in serum-free medium (SFM) for 48 or 72 h and the cell supernatant was collected as secretome (S48 and S72). After collection of secretome, cells were characterised for the expression of MSC phenotypic markers and transcription factors to determine the effect of SFM on these markers. The levels of transforming growth factor-β1 (TGF-β1), interleukin-10 and interleukin-6 in the secretome and the proliferative potential of secretome on chondrocytes were determined.

Results
Our results indicated that SHED exhibited *in vitro* chondrogenic, osteogenic and adipogenic differentiation. Protein and gene expressions showed that the chondrogenic differentiated SHED expressed cartilage cell markers such as aggrecan and collagen type 2. Flow cytometric analysis showed that SHED highly expressed mesenchymal stem cell (MSC) markers (CD44, CD70, CD90, and CD105) and were negative for hematopoietic markers. Interestingly, the expressions of these markers were not significantly different between SHED cultured in complete culture medium (CCM) and SFM for 48 or 72 h. Furthermore, dfferential subcellular localisation of NANOG, OCT4 and SOX2 was observed with OCT4 being localised to the cytoplasm. NANOG was detected in the nucleus and perinuclear, whereas SOX2 was localised to both the cytoplasm and nucleus. However, the expression patterns of these transcription factors between SHED cultured in CCM and SFM were similar. TGF-β1 and IL-6 levels were higher, whereas IL-10 level was lower in S72 as compared with S48. The rate of chondrocyte proliferation incubated in CCM at 24, 48 and 72 h were not significantly different (p<0.05) when compared with S72.

Conclusion
SHED demonstrated multi-lineage differentiation capacity and expressed the markers of pluripotency with differential subcellular localisation. Cultivation of SHED in SFM for production of secretome did not cause any changes to MSC phenotype and secretome was able to promote chondrocyte proliferation.

Keywords

Chondrocyte, secretome, SHED, pluripotency, cytokine

ORAL-12

REGULATORY CHALLENGES IN CLINICAL TRANSLATION OF STEM CELL TECHNOLOGY IN MALAYSIA

[*1] Nishakanthi Gopalan and Mohd Salim Mohamed

[1] Department of Science & Technology Studies, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction

Clinical trials involving stem cell (SC) in Malaysia began in 1987 with its first bone marrow transplantation performed in University Malaya Hospital. It has improved considerably since with over 3626 transplantations but regulation has remained undeveloped over 31 years. The dormancy is exploited by private entities advertising and offering SC therapies without approvals. This study highlights the consequences of the dormant SC regulatory practice concerning bench to bedside and reviews the possible effects expected during the transition towards the new law beginning in 2021.

Methodology

The study employed in-depth interview (IDI) of SC scientists (Malaysian & international) and policymakers and reviewed relevant literature (i.e. articles and government documents retrieved from the many agencies within Ministry of Health (MOH)).

Results

Research hindrance was identified among Malaysian scientists due to unclear regulation, whereas the international scientist explicitly identified clinical translation as the main challenge in SC which is evidently due to regulatory balance in their country, unlike Malaysia. In Malaysia, the unproven SC therapies are predominant in the private sector and despite required to submit advertisements and proposal for approval, some neglect questioning the efficacy and safety of these trials which is a regulatory problem.

Discussion

The ambiguity of overlapping jurisdiction and grey areas within the SC guideline that lack legal stature is exploitative leading to many trials and products not listed in several platforms but advertise in social media, news portals, and websites. The National Pharmaceutical Regulatory Agency (NPRA) documentation in 2016 will regulate cell and gene therapy products with integrated laws but will commence in full-effect beginning in 2021 leaving room for exploitations.

Conclusion / Summary

The right regulative solution is key in solving the ethical issues concerning bench to bedside translation involving patients. While guidelines are available, weak enforcement and oversight in the absence of law will continue to exploit the grey areas which is possible until 2021. We hope this study will facilitate a broad understanding of ethical and legal aspects of SC technology to effectively address the regulatory challenges of emerging technologies like SC.

Keywords

stem cell, unregulated, clinical, translation, policy

ORAL-13

MG63 HUMAN OSTEOBLAST TUMOR CELLS EXHIBIT DIFFERENT BEHAVIOR WHEN TREATED WITH ENCAPSULATED SIMVASTATIN PLGA MICROSPHERES: A MORPHOLOGICAL STUDIES.

[*1,2,3]Nur Aliana Hidayah Mohamed, [2]Andrew Morris, [2]Nashiru Billa and [1]Kevin Shakesheff

[1]School of Pharmacy, The University of Nottingham, Park Campus, Nottingham NG7 2RD, United Kingdom
[2] School of Pharmacy, The University of Nottingham Malaysia Campus, 43500 Semenyih, Selangor, Malaysia.
[3] Oral Maxilofacial Cancer Research Group, Faculty of Dentistry, UiTM Sungai Buloh Campus, Jalan Hospital, 47000 Sungai Buloh.

Introduction
Simvastatin (SIM), a widely used cholesterol-lowering drug, also exhibits tumor-suppressive potentials in several types of malignancy. The statin family of drugs preferentially triggers tumor cell apoptosis by depleting mevalonate pathway metabolites farnesyl pyrophosphate (FPP) and geranylgeranyl pyrophosphate (GGPP), which are used for protein prenylation, including the oncoproteins of the RAS superfamily. Direct treatment of simvastatin potentially showed toxicity in bone tumor. By encapsulating SIM in microspheres, the drug delivery with sustained release and less toxicity can be achieved.

Methodology
The preparation of SIM-loaded microparticles was based on solvent evaporation. Subsequently, the MG63 human osteosarcoma cells were cultured in the presence of SIM-loaded microparticles for 24, 48 and 72 hours, and their proliferation was assessed by MTT assay. Cells grown in blank microparticles served as the control. Upon the treatment, cells from the culture were prepared for light, fluorescent and scanning electron microscopy studies.

Results
Interestingly, cultured MG63 cells showed apoptotic effects from 0.097mg/ml to 0.4 mg/ml however starting to increase proliferation from 0.4 mg/ml to 12.0 mg/ml. Results showed spheroid morphology with numerous secretion vesicles accumulated on the surface, observing no cytoplasmic projections with intercellular connections. Cells cultured with simvastatin encapsulated microparticles between the concentration of apoptotic effects had a polygonal and spindle-shaped morphology, with cytoplasmic projections that interconnected cells.

Discussion
The apoptotic effect of SIM-loaded microparticles was significant at the early treatment and increased as the concentration of the microparticles increased. The morphologically destructed MG 63 was reverted by SIM-loaded microparticles. This may suggest the potential of SIM-loaded microparticles in cell stress and stabilizing the osteogenic renewal processes. However, as the concentration increased, the cellular activities was less sensitive and contributed to the proliferation of MG 63 cells. Interestingly, these proliferated cells produce an accumulation of cytosolic lipid droplets which indicate antiproliferative effects in malignant cells.

Conclusion / Summary
SIM-loaded microparticles, in the context of bone production, preservation and remodeling, therefore function as modulator of osteoclastogenesis/osteogenesis. In addition SIM-loaded microparticles could also potentially inhibit human osteosarcoma. However modification and optimization is required to achieve the apoptotic effects from the SIM-loaded microparticles.

Keywords
Simvastatin, SIM-loaded microparticles, anticancer, osteoclastogenesis/osteogenesis.

ORAL-14

REVERSAL OF DRUG-RESISTANCE MECHANISMS IN LIVER CANCER CELLS USING LOW-DOSE ULTRA-SMALL SIZE GOLD NANOPARTICLE-TAGGED ANTI-CANCER DRUG

Aleem Ahmed Khan, Sandeep Kumar Vishwakarma, Avinash Bardia, Syed Ameer Basha Paspala, and Md. Aejaz Habeeb

[*1]Central Laboratory for Stem Cell Research and Translational Medicine,
Centre for Liver Research and Diagnostics, Deccan College of Medical Sciences, Kanchanbagh, Hyderabad-500058, Telangana, India

Introduction
Existing treatment for liver cancers largely fail due to the chemo résistance properties of cancer cells. High doses of drugs lead to systemic toxicity resulting in a multitude of unwanted adverse reactions due to their lack of availability at tumor site, poor tumor intake of drugs and rapid elimination. In present study, we investigated the effect of tagged anti-tumor drugs with ultra-small gold nanoparticles to investigate their effect on drug-resistant liver cancer cells.

Methodology
We developed a stable colloidal suspension of sorafenib-gold nanoconjugate (SF-GNP) of <10 nm size in aqueous medium for reverting the cancer drug resistance in SF-resistant liver cancer cells in a 3D ex-vivo model system. Quantitative estimation of the amount of SF binds on GNP was performed by HPLC. SF-resistant tumor cell colonies were developed in soft-agar by consistent exposure to IC50 dose of SF up to seven passages. Changes in colony number and cell death were identified post-nanoconjugate exposure to SF-resistant colonies and compared with the untreated groups.

Results
In vivo biocompatibility assay of SF-GNPs showed absence of systemic toxicological effects including hematological, biochemical and histological parameters. SF-GNP nanoconjugates significantly reduced (>80%) the percentage cell survival and the size and number of SF resistant solid tumor colonies of liver cancer cells in 3D model system. The exposure of SF-GNP nanoconjugate to SF resistant liver cancer cell colonies also provided evidence for anti-proliferative effect and reversal of drug resistance by elucidating the molecular regulatory mechanisms of extracellular matrix factor, tumor growth factor, hURP and drug transporter.

Discussion
This novel nano-formulation does not induce adverse effects in the body and kills drug resistant cancer cells by specific targeting at very low dose. The approach is cost-effective and can treat both solid cancers and drug resistant cancers.

Conclusion / Summary
This particular strategy of using SF-GNP conjugate in treating SF resistant liver cancer cells may augment the possibility of SF and related drugs to reduce the load of drug resistance with lower dose and reduced adverse events in advanced cancer.

Keywords
Cancer drug resistance; Gold nanoparticles; Drug toxicity; Reversal of drug resistance; Drug transporters

ORAL-15

BIASED SIGNALLING VIA TLR4 MODULATES THE STEMNESS, PROLIFERATION, MIGRATION, AND DIFFERENTIATION OF GLIOMA CANCER STEM CELLS

Yiming Meng[1,#], Marie-Theres Zeuner[1], Graeme S Cottrell[2] and Darius Widera[1,*]

[1]Stem Cell Biology and Regenerative Medicine, School of Pharmacy, University of Reading, Reading, RG6 6AP, United Kingdom
[2]Cellular and Molecular Neuroscience, School of Pharmacy, University of Reading, Reading, RG6 6AP, United Kingdom

Introduction
Toll-like receptors (TLRs) are type I integral membrane proteins and essential pathogen recognition receptors that function in innate immune system. MyD88-dependent pathway and MyD88-independent pathway are two major signalling pathways triggered by TLRs, and Toll-like receptor 4 is the only member of TLRs that can trigger both. Depending on the ligand, signalling via Toll-like receptor 4 (TLR4) can either activate the pro-inflammatory transcription factor 'Kappa-light-chain-enhancer' of activated B cells (NF-κB) or the anti-viral and anti-inflammatory interferon regulatory factor 3 (IRF3) biased. In cancer cells, NF-κB and IRF3 have been described to have opposing effects. In this study, we wanted to understand the ligand-specific molecular mechanisms of biased signalling via TLR4 in glioma cells. Specifically, we aimed to address the impact of TLR4 mediated biased signalling on the stemness, proliferation, migration, differentiation and survival of glioma cancer stem cells (GCSCs) and hypothesised that IRF3-biased TLR4 agonists will reduce the stemness and proliferation whereas NF-κB-biased agonists will have opposite effects.

Methodology
As a model cell line for GCSCs, we used the glioblastoma cell line U251-MG. Multiple biochemical technologies were used, including immunocytochemistry, flow cytometry, immunocytochemistry, Western blot, RT-PCR, ELISA. In addition, tumourisphere formation was used to increase the proportion of CD133 positive GCSCs in U251 cells followed by MACs sorting. GCSCs ($CD133^+$) and non-GCSCs U251 ($CD133^-$) were studied respectively after treatment with LPS of *Escherichia coli* origin (LPS_{EC}), and LPS of *Salmonella minnesota* (LPS_{SM}). Proliferation assays, cell viability assays and wound healing assays were also used to illustrate the activation of MyD-88 dependent signalling via TLR4.

Results
We were able to confirm that U251 express TLR4 and the downstream adapter molecules required for TLR4 activation, and the IRF3 and NF-κB activation kinetics and dynamics are ligand dependent. LPS_{EC} activates NF-κB-based MyD88-dependent downstream signalling, and increases proliferation and stemness whereas LPS_{SM} predominantly activates MyD88-independent pathway and inhibits cell migration and increases the differentiation GCSCs.

Conclusion
NF-κB biased TLR4 ligands increase the proliferation and stemness of GCSCs; whereas IRF3 biased TLR4 ligands drive differentiation and inhibit migration of GCSCs.

Key words
Glioma cancer stem cells, TLR4, NF- κB, cell behaviour.

LIST OF ABSTRACTS FOR POSTER PRESENTATION

POS-01

KNOWLEDGE, AWARENESS AND PERCEPTION OF HEALTHCARE PROFESSIONALS REGARDING CORD BLOOD STEM CELLS BANKING

Ong Heng Seng[1], Farahnaz Amini[1*]

[1]School of Healthy Aging, Medical Aesthetics, Regenerative Medicine, Faculty of Medicine and Health Sciences, UCSI University

Introduction
Umbilical cord blood (UCB) is an alternative and non-invasive to bone source of hematopoietic stem. Healthcare professionals are expected as the front-line of educating public about UCB. However, there are limited studies regarding Malaysian health professionals' knowledge, awareness and perception towards UCB. This study was aimed at assessing awareness, knowledge and perception of UCB banking in Malaysian healthcare professionals.

Methodology
A survey was done using a questionnaire with a total of 39 questions, of which 16 questions measured the level of knowledge. Every correct answer was given 1 point, expecting the total score to range from 0 to 16. Educational brochures were distributed among participants. Recruitment was done in a few hospitals in Kuala Lumpur in accordance with the set inclusion and exclusion criteria following ethics approval.

Results
The response rate was 79% (198 out of 250). About 57% were doctors and 43% nurses. Majority of them were in the age group of 25-30 years (46%), female (61%), Malay (48.5%) and 51% degree holder. Only 34% of them get to know about UCB banking from healthcare providers. A marginally significant association was found between level of awareness and marital status ($p = 0.054$), level of awareness and yes-answers to the question "have you heard about UCB banking" ($p<0.001$), and level of knowledge and No-answers to the question "have you heard about UCB banking" ($p<0.001$).

Discussion
Unlike western countries, in Malaysia, most of the information received by healthcare professionals on UCB banking is from private UCB banks. Educating healthcare professionals may help to make an informed choice regarding banking or donating UCB.

Conclusion / Summary
Healthcare professionals in this study have poor level of awareness and knowledge about UCB banking. Knowledge and awareness seemed to have a direct effect on the perception of participants and reflected in their choice of UCB banking and donation.

Keywords
Awareness; Cord blood stem cells banking; Healthcare Professionals; Knowledge; Perception

POS-02

BASIC FIBROBLAST GROWTH FACTOR ENHANCES THE EXPANSION AND SECRETORY PROFILE OF HUMAN PLACENTA-DERIVED MESENCHYMAL STEM CELLS

Shalini Vellasamy [1,2,*],Sharmili Vidyadaran [2], Elizabeth George [3], Rajesh Ramasamy [2]

[1]Department of Microbiology, Faculty of Medicine and Biomedical Sciences, Mahsa University, Bandar Saujana Putra, 42610 Jenjarom, Selangor, Malaysia.
[2] Immunology Laboratory, Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia.
[3] Haematology Unit, Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia.

Introduction
Mesenchymal stem cells (MSCs) hold a great therapeutic potential for regenerative medicine and tissue engineering due to inherent immunomodulatory and reparative properties. Hence, it necessitates a readily available supplyof MSCs to meet the clinical demands adequately. Although, a human placenta can produce MSCs, the in vitro culture-mediated cellular senescence often affect the quality of cell product. Thus, the current study has explored the feasibility of basic fibroblast growth factor (bFGF) to enhance the growth of placenta-derived MSCs (PLC-MSCs).

Methodology
The basic fibroblast growth factor (bFGF) was supplemented to optimise the growth of MSCs. The effects of bFGF on morphology, growth kinetics and cytokine secretion of PLC-MSCs were assessed.

Results
The bFGF supplementation increased the proliferation of PLC-MSCs in a dose-dependent manner and 40 ng/ml showed a high trophism effect on PLC-MSC's growth. In the presence of bFGF, PLC-MSCs acquired a small and well-defined morphology that reflect an active proliferative status. BFGF has induced PLC-MSCs to achieve a shorter doubling time (45 hrs) as compared to the non-supplemented PLC-MSCs culture (81 hrs). Furthermore, bFGF impelled PLC-MSCs into cell cycle machinery where a substantial fraction of cells was driven to S and G2/M phases. Amongst, 36 screened cytokines; bFGF had only altered the secretion of IL-8, IL-6, TNFR1, MMP3 and VEGF.

Discussion
MSCs were successfully generated from placenta by using a novel method that combines enzymatic digestion and mechanical dissociation that found to be efficient compared to the explant or the enzymatic digestion method. There were significant differences between the bFGF-supplemented and non-supplemented MSC cultures regarding their appearance and colony formation ability. Also, bFGF enhanced proliferation of MSCs accompanied by a steady progression of cell cycle and delayed senescence MSCs. The modulation of several inflammatory cytokines suggest that could MSC supports the notion of being an bio immunosuppressant.

Conclusion / Summary
The present study showed that bFGF supplementation promotes the growth of PLC-MSCs without significantly deviating from the standard criteria of MSCs. Thus, bFGF could be considered as a potential mitogen to facilitatethe large-scale production of PLC-MSCs.

Keywords
Basic fibroblast growth factor, Placenta, Mesenchymal stem cells, Cell cycle, Cytokine secretion

POS-03

HLA ANTIGEN AND HAPLOTYPE DISTRIBUTION IN MALAYSIAN CANDIDATES FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION

Tey KWF[1], Bee PC[2], Ng KP[2], Shanmugam H[3], Zain SM[1], Eng HS[1]

[1] Department of Pharmacology, University of Malaya
[2] Department of Medicine, University of Malaya
[3] Department of Pathology, University of Malaya

Introduction

Histocompatibility matching of human leukocyte antigens (HLA) between recipient and their family members is essential to identify suitable donors for allogeneic hematopoietic stem cell transplant (AHSCT). Data on HLA antigen and haplotype frequencies may allow better prediction of the probability of finding HLA-matched donors, consequently enhance the donor search strategy. This study aims to determine the distribution of HLA antigens and haplotypes in patients who had undergone HLA typing for AHSCT in University of Malaya Medical Centre and to review the outcome of the transplant. To our knowledge this is the first haplotype frequency report in Malaysia.

Methodology

This retrospective study involves the analysis of HLA typing results of patients and their potential donors who had undergone HLA matching in University of Malaya Medical Centre (UMMC) from 2003 to 2017. The patients and donors' HLA typing results were collected through their laboratory reports. The Centre routinely tests for HLA antigen/allele group by intermediate resolution solid phase assay. Only the siblings of the patients were tested in view of the patient require full HLA matched donor for transplantation. HLA typing for HLA-A, -B, -DR, and -DQ from each patient and potential donor were collected to derive the haplotype present in the patient's family. The frequency of recurring haplotype and antigen present was then directly counted and recorded. Recurring haplotype and antigen present within a family were counted as 1 unit to the overall haplotype and antigen frequency.

Results

A total of 143 patients and their family members (mean no. of siblings = 2.7, SD ± 1.4) were recruited for this study. Majority of the patients were Chinese (62.9%), followed by Malay (29.4%), and Indian (4.9%). While, 81 (56.6%) found HLA-matched donors, however only 42 (29.4%) patients proceeded with AHSCT. Majority of the Malays found a match within their family (69%), followed by Indians (57%), and Chinese (52%). 53%, 52%, and 25% of Chinese, Malays, and Indians respectively from the matched group proceeded with transplant. No significant association was found between number of siblings screened and number of HLA-matched siblings ($p = 0.71$). Of the 42 patients who proceeded for AHSCT, 44 haplotypes were successfully derived from 11 patients and their families. Of the 44 haplotypes determined, 6.8% were haplotype HLA-A*33-B*58-DRB1*17-DQB1*02, while HLA-A*33-B*58-DRB1*13-DQB1*06, HLA-A*24-B*75-DRB1*12-DQB1*07, HLA-A*02-B*60-DRB1*09-DQB1*09, HLA-A*02-B*46-DRB1*16-DQB1*05, HLA-A*02-B*13-DRB1*15-DQB1*06 were each 4.5% respectively. No disease relapse occurred within the haplotype determined group, however one death was reported post-transplant. The most frequent antigens observed from the patients and their families of the transplanted group was HLA-A*11 (18.2%), HLA-B*58 (15.9%), HLA-DRB1*12 (13.6%), and HLA-DQB1*06 (18.2%).

Conclusion

Malaysia is comprised of a multi-ethnic population in which the haplotype distribution may vary among ethnic groups. Though the results suggested the six most common haplotypes, a larger scale study in healthy population shall be performed to validate the findings.

Keywords

Haplotype Frequency, Allogeneic Hematopoietic Stem Cell Transplant, Human Leukocyte Antigen

POS-04

EFFECTS OF CURCUMIN ANALOGUE DK 1 ON THE APOPTOTIC PROCESS OF BONE CANCER CELL LINE *IN VITRO*

Muhammad Nazirul Mubin Aziz[1], Noorjahan Banu Alitheen[1*], Cheah Yoke Kqueen[2], Mas Jaffri Masarudin[1], and Nadiah Abu[3]

[1] Department of Cell and Molecular Biology, Faculty of Biotechnology and Biomolecular Science, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia.
[2] Department of Biomedical Science, Faculty of Medicine and Health Science, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia
[3] UKM Medical Molecular Biology Institute (UMBI), UKM Medical Centre, 56000 Cheras, Kuala Lumpur, Malaysia

Introduction
Osteosarcoma (OS) is the most prevalent malignant bone cancers among children and adolescents. Even with intensive treatment the patients' survival rate will drop significantly to 30% if diagnosed with malignant OS. Therefore, discovery of novel anti-osteosarcoma agent from natural products that is pharmacologically safe for consumption is imperative. Curcumin is an active component that is isolated from turmeric and possesses anti-angiogenic, anti-proliferative and low cytotoxic effects on healthy cells. However, dietary curcumin has poor circulating bioavailability in vivo which leads to the development of chemically synthesised curcuminoid analog, namely (Z)-3-hydroxy-1-(2-hydroxyphenyl)-3-phenylprop–2–en-1-one (DK1). Thus, this study is executed to examine the cytotoxic and apoptosis mechanism of DK1 against OS.

Methodology
In this study, MTT was used to investigate the cytotoxic effect of DK1 in U-2 OS cells. Then, AO/PI double staining was applied to examine the cell death microscopically. Flow cytometer analysis; including Annexin V/FITC, cell cycle analysis and JC-1 were incorporated to determine mode of cell death and further mechanism was elucidated using qRT-PCR and proteome profiler to quantify the expression of apoptotic-related genes and proteins.

Results
The results indicated that DK1 successfully inhibited the cell proliferation in U-2 OS with IC_{50} values of 19.6µM. DK1 also induced morphological changes in the DK1 treated cell that showed apoptosis features. S phase cell cycle arrest can be observed in U-2 OS and increased of Sub G0/G1 population that indicates apoptosis occurrence. These results are supported by increased expression of several pro-apoptotic genes and proteins like caspase-3, caspase-9 and BAX.

Discussion
Based on the results, it suggest that curcumin analog DK1 induced mitochondrial signaling pathway proved by up-regulated expression of pro-apoptotic genes and proteins such as caspase-3, caspase-9, BAX and Cytochrome C. Moreover, DK1 also inhibited anti-apoptosis protein like HO-1/HMOX1/HSP32 which provides a cytoprotective effect for cancer cells against apoptosis.

Conclusion / Summary
In conclusion, DK1 could be considered as a potential candidate for anti-osteosarcoma agent in near future as it is able to induce apoptosis via mitochondrial signaling pathway in U-2 OS osteosarcoma cell line.

Keywords
Osteosarcoma (OS), Curcumin analog DK1, Metastasis, Apoptosis, Mitochondria-dependent

POS-05

ESTABLISHMENT OF RENAL CANCER EPITHELIAL AND FIBROBLAST CELL LINES FROM PRIMARY RENAL TUMOURS

Ning Yi Yap[1*], Teng Aik Ong[1], Christudas Morais[2], Jayalakshmi Pailoor[3], Glenda C. Gobe[2], Retnagowri Rajandram[1]

[*1] Department of Surgery, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur, Malaysia
[2] Centre for Kidney Disease Research, the University of Queensland Diamantina Institute, The University of Queensland, Brisbane, Australia
[3] Department of Pathology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction
Renal cell carcinoma (RCC) is one of the most lethal urogenital cancers with poor prognosis in metastatic cases. The reason for this is most patients with metastatic RCC develop intolerance to drug related toxicities or resistance to targeted therapies. Cell lines are valuable resources for the in-vitro investigation of molecular and genetic imbalances leading to renal carcinogenesis and are essential for evaluating cellular drug response or toxicity. We have developed a simple and rapid protocol of establishing epithelial and fibroblast cell lines from renal cancer nephrectomy tissue.

Methodology
Nephrectomy tissue collected from the operation theatre was processed by mechanical disaggregation, collagenase digestion and cell sieving for establishing epithelial cells while fibroblast cells were grown from explants. The protocol was a modification from published reports with additional antibiotics and washing steps added to eliminate yeast/mold, bacterial and mycoplasma contamination from the surgical source. Cell characterization for epithelial or fibroblast markers was performed using immunofluorescence and quantitative PCR.

Results
Eleven stable epithelial renal tumour cell lines of various subtypes, including clear cell RCC (ccRCC), ccRCC with sarcomatoid transformation, undifferentiated RCC with some papillary features and non-RCC Ewing's sarcoma were established with a spontaneous immortalization rate of 21.6%. Normal kidney cells did not achieve spontaneous immortalization and senesced after 3-5 passages. Eight fibroblast cell cultures grew successfully but did not achieve spontaneous immortalization. Cells of epithelial origin exhibited higher expressions of epithelial markers such as pan-cytokeratin, cytokeratin-8 (CK8) and E-cadherin whereas fibroblast cells expressed high α-smooth muscle actin (α-SMA) and fibroblast activation protein (FAP).

Discussion
This protocol allows for simultaneous establishment of RCC, normal kidney and RCC associated fibroblast cell lines or cultures from nephrectomy tissue samples with successful spontaneous immortalization for some RCC epithelial cell lines. Morphological, immunofluorescence and qPCR characterization can be carried out to determine the epithelial or fibroblastic origin of the cells.

Conclusion
Cell lines established here originated from Asian or Malaysian patients and may more accurately represent the molecular characteristics of our population compared to commercial cell lines which are usually established from Caucasian patients. In addition, rare kidney tumour subtypes were successfully established from this study.

Keyword
Cell lines, fibroblast, epithelial, renal cell carcinoma

POS-06

NEW METHOD FOR CANCER CELL DETECTION BASED ON SHIFTED ANGLE OF POLARIZATION

Salmah Binti Karman, Siti Nurainie Tukimin, Mohd Yazed Ahmad and Wan Safwani Wan Kamarul Zaman

Department of Biomedical Engineering, Faculty of Engineering, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction

Physician go through preliminary tests for early inspection either by clinical biopsy for tissue sample discrimination, immunoassay for in situ determination of Ag-Ab complex or most probably by electrochemistry biosensor for quantitative biomarker detection. Current development of optical biosensor possibly ideals for sensitive, selective and label free nothing simplest but burdensome and sophisticated. Their study of interest relying more on nanomaterial (indirect biochemical assay) application rather than directly test for in situ discrimination between normal and cancer cells that would be inspired from density regulation of salts using Polarized Light (PL) based sensor in this study.

Methodology

Two spectrum of light sources (Green (495-570nm) and Red (620-750nm)) are let to pass through different density of salt solutions (density range of 1.006-1.201g/ml). The shifted angle of polarization (AOP) are monitored using PL sensor (Figure 1).

Results

RED spectrum with salt density (range of 1.006-1.193g/ml) shifted AOP value with increasing trend with correlation coefficient of 0.902 and significant value of p=0.006. As for the GREEN spectrum, the increment of the shifted AOP holds higher correlation coefficient (R=0.923) and better significant value of p=0.003 under same range of salt density (Figure 2).

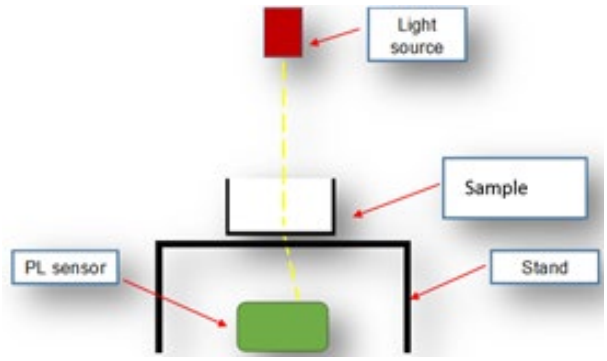

Figure 1: Apparatus setup for the

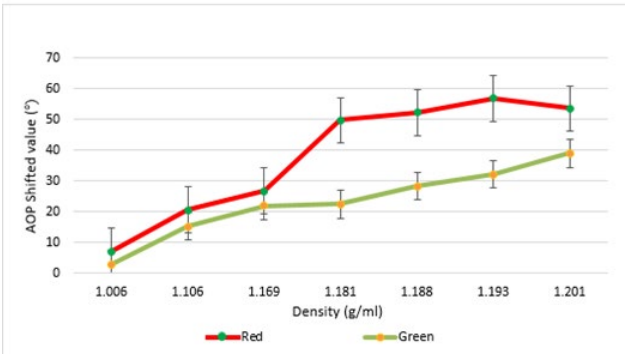

Figure 2: AOP Shifted value according

Discussion

Based on the results, the green spectrum hold better correlation compare to the red spectrum. The shifted AOP value increased as the density of salt increased. Based on this finding, cancer cell which hold higher density of organelles would experience trend.

Conclusion

Therefore, PL sensor with shifted AOP parameter could be utilized for detecting cancer cell.

Keywords
Cancer detection, Angle of Polarization, Polarized Light Sensor

POS-07

ANTICANCER EFFECTS OF TOCOTRIENOLS – FROM BENCH TO BEDSIDE

Puvaneswari Meganathan[1,2,3], Retnagowri Rajandram[1], Zamri Chik[2] and Nur Aishah Taib[1]

[1] Department of Surgery, [2] Department of Pharmacology,
Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia
[3] Malaysian Palm Oil Board, No. 6 Persiaran Institusi, Bandar Baru Bangi, 43000 Kajang, Selangor, Malaysia

Introduction

Rising cases of breast cancer with estimated new cases in 2018 being 266,120 has been a vastly discussed topic among health practitioners, pharmaceutical industries and general public. The increasing cost of treatment and undeniable adverse effects often seen with conventional therapies has shifted the attention towards multidisciplinary approach and personalised treatment. In addition to cancer, the alarming rate of other lifestyle related diseases has also contributed to the increased awareness towards nutraceuticals that are natural derivative from plants. These multi-targeted nutraceuticals are gaining prominence in the battle against cancer which is a multifactorial disease. Curcumin, resveratrol and tocotrienols are among the natural compounds that have been studied in line with the concept "from bench to bedside". Among these nutraceuticals, tocotrienols being a member of vitamin E family has been studied in depth in the last 3 decades. However, alpha-tocopherol which is a lesser potent isoform, is often mistaken as a general term for Vitamin E, thus making tocotrienols as the unsung heroes in anti-cancer research despite their beneficial biological properties. Till date, more than 40 clinical trials involving tocotrienol supplementation in various disease conditions have been published with no serious adverse events being reported. Moreover, encouraging results have been observed in two clinical trials involving breast and pancreatic cancer patients. Although these studies were successful in answering many queries and scepticisms pertaining to tocotrienol supplementation, however, bioavailability of tocotrienols in humans has been a debated issue. Despite emerging new studies showing evidence that circulating plasma tocotrienol levels are sufficient to evoke therapeutic response, more clinical studies are warranted to convince the scientific community, clinicians and healthcare authorities on the potential roles of tocotrienols. Based on these literatures, we aim to bridge the gap between the pre-clinical and clinical findings of tocotrienols as potential anti-cancer agent. We have completed a phase 1a bioavailability and pharmacokinetics study that shows sufficient plasma concentrations of tocotrienols can be achieved in healthy subjects supplemented with oral tocotrienol formulations after feeding them with standardized diet. Following these, a maximum tolerated dose (MTD) study will be carried out in pre-surgical women with breast cancer to determine the safest and most tolerable dose.

Keywords

Cancer, Tocotrienols, Breast Cancer, Clinical trial, Nutraceutical

POS-08

THE EXPRESSION AND SIGNIFICANCE OF H3 LYSINE 27 (H3K27) DEMETHYLASES IN RENAL CELL CARCINOMA (RCC).

Rebecca Anthony[1], Retnagowri Rajandram[1], Man Kein Seong [2] and Shanggar Kuppusamy[1]*

[*1] Department of Surgery, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur, Malaysia
[2] Department of Pathology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction
The histone H3K27 demethylases UTX and JMJD3 are important proteins/enzymes that could regulate gene expression by changing the physical state of chromatin. Active and inactive regions of the genome are determined through lysine methylation. Abnormal H3K27 methylation has been implicated in carcinogenesis of tumors but the expression of H3K27 demethylases in renal cell carcinoma (RCC) is still unclear. Therefore, this study was designed to investigate the expression patterns of UTX and JMJD3 in RCC from a local cohort.

Methodology
Clear cell RCC (ccRCC) patients who underwent nephrectomy in Urology Unit, University of Malaya Medical Centre (UMMC) from 2011 till 2018 were recruited retrospectively. However only 35 ccRCC patients formalin-fixed paraffin-embedded (FFPE) tissues were obtained from UM Pathology based on availability. UTX and JMJD3 protein expression were assessed by immunohistochemical analysis on FFPE tissues.

Result
UTX and JMJD3 were positively stained ccRCC cancerous tissues compared to adjacent normal kidney and control colon tissues. H3K27 demethylases are localized mainly in the nucleus of ccRCC tissue.

Discussion
The results suggest the presence of both UTX and/or JMJD3 could be linked with the progression of ccRCC. Assessing for UTX and JMJD3 expression by IHC may be diagnostically useful for ccRCC.

Conclusion / Summary
Thus both proteins could be biomarkers in the early diagnosis of ccRCC which need to be further explored.

Keywords
Renal cell carcinoma, histone H3K27 demethylases, UTX, JMJD3, immunohistochemistry

POS-09

MICRORNA AND DOWNSTREAM MRNA GENE EXPRESSION PROFILING OF PUTATIVE CANCER STEM CELLS ISOLATED FROM CANINE MAMMARY ADENOCARCINOMA CELLS WITH DOXORUBICIN RESISTANCE.

Gayathri Thevi Selvarajah[1*], Kabiru Sahabi[1], Cheah Yoke Kqueen[2], Mokrish Ajat[1]

[*1] Faculty of Veterinary Medicine & [2]Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia, 43400 UPM Serdang, Malaysia.

Introduction

Canine mammary gland tumour (CMT) is one of the naturally developed cancer in female dogs. Cancer stem cells (CSCs) are able to initiate tumour development, metastasis and facilitate recurrence due to properties such as self-renew, longevity, resistance to radiotherapy and chemotherapy, undergo a dormant state, ability to differentiate and evade apoptosis. MicroRNA (miRNA) are short non-coding RNA that can inhibit the translation of messenger RNA (mRNA) to protein in multicellular organisms; where majority of all mRNA are predicted to be under the control of miRNA. The objective of this study is to determine the miRNAs and downstream target mRNAs in CSC of canine mammary adenocarcinoma cell lines with differing doxorubicin sensitivity.

Methodology

A doxorubicin-resistant subline (CMT-Star) was developed from CMT-Stylo (parent canine mammary adenocarcinoma cell line). Allophycocyanin conjugated-CD44 and R-Phycoerythrin conjugated-CD24 antibodies were used to sort putative CSC using flow cytometry. QPCR was performed for ALDH marker on the sorted cells. MiRNA profiling was done using Agilent SurePrint®G3 Agilent Custom canine specific miRNA 8x60K array and data analysed for signalling pathways, biological and cellular processes using GeneSpring®.

Results & Discussion

The isolated putative CSCs were $CD44^{+}$, $CD24^{-/low}$ and $ALDH^{+}$. A total of 6 miRNAs were differentially expressed (4 upregulated and 2 downregulated) in the CSC from CMT-Stylo and at fold change of 2.0, 154 mRNAs were identified. A total of 14 miRNAs were differentially expressed (7 upregulated and 7 downregulated) in the CSC isolated from CMT-Star and at fold change of 2.0, 263 mRNA were identified. The miRNAs identified in the CSC have major roles in decreased cell proliferation and maintenance of CSC phenotype, including drug resistance. Wnt, EGFR1, TGF beta Receptor Signalling, Toll-like receptor and Type II interferon signalling were among the major pathways regulated by the miRNAs.

Conclusion / Summary

In conclusion, this study has profiled the canine specific miRNA expression within the sub-population of cells with CSC marker expression to enhance understanding the role of CSC in drug resistance in CMT and facilitate development of common therapeutics for human breast cancer based on these novel targets.

Keywords

canine mammary gland cancer, microRNA, microarray, cancer stem cells, doxorubicin resistance

POS-10

A SYSTEMATIC LITERATURE SEARCH OF THE GENETIC ALTERATIONS IN SARCOMATOID RENAL CELL CARCINOMA

Foong Yi Xian, Yap Ning Yi, Retnagowri Rajandram, Ong Teng Aik

Department of Surgery, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.

Introduction
Sarcomatoid renal cell carcinoma (sRCC) is characterized by the presence of a biphasic tumour containing both sarcomatoid components and epithelial elements. sRCC is not classified as a distinct entity of renal cell carcinoma (RCC) because sarcomatoid features are observed in different histologic subtypes, accounting for about 5% of RCC. Even though sRCC is rare, it is highly aggressive as it responds poorly to conventional treatments and portends a dismal prognosis. Previous research suggested that the molecular pathogenesis of sRCC may be different for each histology. In this study, we performed a systematic literature search prior to providing a review on the genetic alterations in different RCC subtypes with sarcomatoid transformation.

Methodology
We extensively searched electronic bibliographic databases including PubMed, EMBASE, The Cochrane Library, Web of Science, CINAHL and Scopus. There were no restrictions for language and publication period for database searching. The search strategy used was (“sarcomatoid" OR "sarcomatous") AND ("kidney" OR "renal") AND ("cancer" OR "carcinoma") AND ("gene" OR "genetic" OR "genome" OR "genomic") AND ("mutation" OR "alteration" OR "aberration" OR "variation" OR "change"). The systematic review protocol was developed and registered on PROSPERO.

Results
2735 records were identified through database searching. 378 duplicates were removed. Following deduplication, the titles and abstracts of 2357 records were screened against the exclusion criteria: non-original articles, non-human studies and not written in English language. 2271 records were excluded. The full-text articles of the remaining 86 records were assessed for eligibility. After full-text screening, 56 records were identified as non-relevant and excluded. 30 studies were selected to be included in the systematic review.

Conclusion / Summary
The risk of bias and the quality of included studies will be assessed using the Newcastle-Ottawa Scale. We will provide a systematic review summarizing the genetic alterations in sRCC according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline.

Keywords
Systematic literature search, sarcomatoid renal cell carcinoma, genetic alterations

POS-11

THE EVALUATION OF LEPTIN AS AN APPROPRIATE BIOMARKER FOR THE EARLY DETECTION OF RENAL CELL CARCINOMA (RCC): A SYSTEMATIC REVIEW AND META-ANALYSIS

Komathi Perumal[1], Weng Kit Huin[2], Ning Yi Yap[1], Teng Aik Ong[1], Glenda Gobe[3], Retnagowri Rajandram[1]

[1] Department of Surgery, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur, Malaysia
[2] Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[3] Centre for Kidney Disease Research, The University of Queensland Diamantina Institute, The University of Queensland, Brisbane, Australia

Introduction
The study was initiated to perform a systematic review and meta-analysis on diagnostic and prognostic value of leptin in renal cell carcinoma (RCC). Leptin is an adipokine that is secreted from adipose tissue. There is growing interest in the study on this adipokine in cancers. Leptin acts as satiety hormone and aids in energy expenditure. However, recent studies link leptin with growth of various cancers including RCC.

Material
Electronic databases, namely PubMed, CINAHL, Web of Science, Science Direct and Google Scholar, were searched to analyze the effect of leptin in RCC. The analysis was done according to PRISMA guidelines for systematic review & meta-analysis. The bias assessment was done for both case control and cohort groups by using Newcastle-Ottawa Scale (NOS). All the selected studies were evaluated for the diagnostic and prognostic value leptin in RCC patients with RevMan version 5.3 software.

Results
Overall, 6 original research studies were included for meta-analysis. Presence of serum leptin levels were inversely proportional to RCC diagnostic value (mean differences 1.39, 95% CI -3.32-6.10, P<0.00001). The level of leptin was also inversely proportional to RCC prognostic value in both Stage and Grade (mean differences 0.82, 95% CI -1.68-3.32, P=0.02 and mean differences 0.07, 95% CI -0.56-0.70, P=0.48), respectively. Level of leptin was not significant in clear cell RCC (ccRCC) compared with non-ccRCC (mean differences -6.41, 95% CI -11.11- -1.68, P<0.00001).

Conclusion
The level of leptin in a patient with RCC is unlikely to be associated with development or progression of RCC. Based on our findings, leptin does not serve as a biomarker for early detection in RCC patients, especially those who are obese. However, there are still unclear underlying mechanisms and limited studies on leptin in RCC, and this warrants further future investigation.

Keywords
Diagnostic Tool, Kidney Cancer, Obesity, Prognostication, Risk Factor

POS-12

PROTEIN PROFILING OF LOW, INTERMEDIATE AND HIGH-RISK ENDOMETRIAL CARCINOMA: DISCOVERY AT UNIVERSITY OF MALAYA

Si Lay Khaing[1], Intan Sofia Omar[2], Thamil Selvee Ramasamy[3], Lim Chung Keat[1], Noor Azmi Mat Adenan[1], Siti Zawiah Omar[1]

[1]Department of Obstetrics & Gynaecology,
[2]Department of Pharmacology,
[3]Department of Molecular Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

Introduction
Endometrial Cancer(EC) is the sixth most commonly diagnosed women cancer worldwide and third common gynaecological cancer in Malaysia. Our aim is to determine the different protein-expression profiling in high risk endometrial cancer patients compared to low and intermediate risk endometrial carcinoma in our multi-ethnic Malaysian population.

Methodology
Archived samples, three with low-intermediate risk and one with high risk poorly differentiated EC from peri-menopause and postmenopausal women were obtained from BioBank, University of Malaya, and were studied at High Impact research Laboratory, University of Malaya. Total RNA from Fresh frozen Paraffin Embedded (FFPE) samples were extracted using RNEasy Mini Kit (Qiagen, Valencia, CA). The integrity of total RNA was checked with Bio analyser. The protein profiling were performed using nCounter Pan Cancer Pathway Panel and Protein Kit (Solid Tumor Signaling proteins).

Results
Total solid tumour signaling 26 proteins were analysed from 4 samples. In high- risk poorly differentiated EC, all proteins were found to be highly expressed compared to low- intermediate risk EC (Figure1). Among these proteins, Ki-67, Met (D1C2) and Phospho-PDK1 are much higher in high risk EC compared to low risk EC.

Conclusion
Therefore, the protein-expression profiling of endometrial cancer will be useful to determine the therapeutic modality for treatment of endometrial cancer for best outcome in personalized medicine.

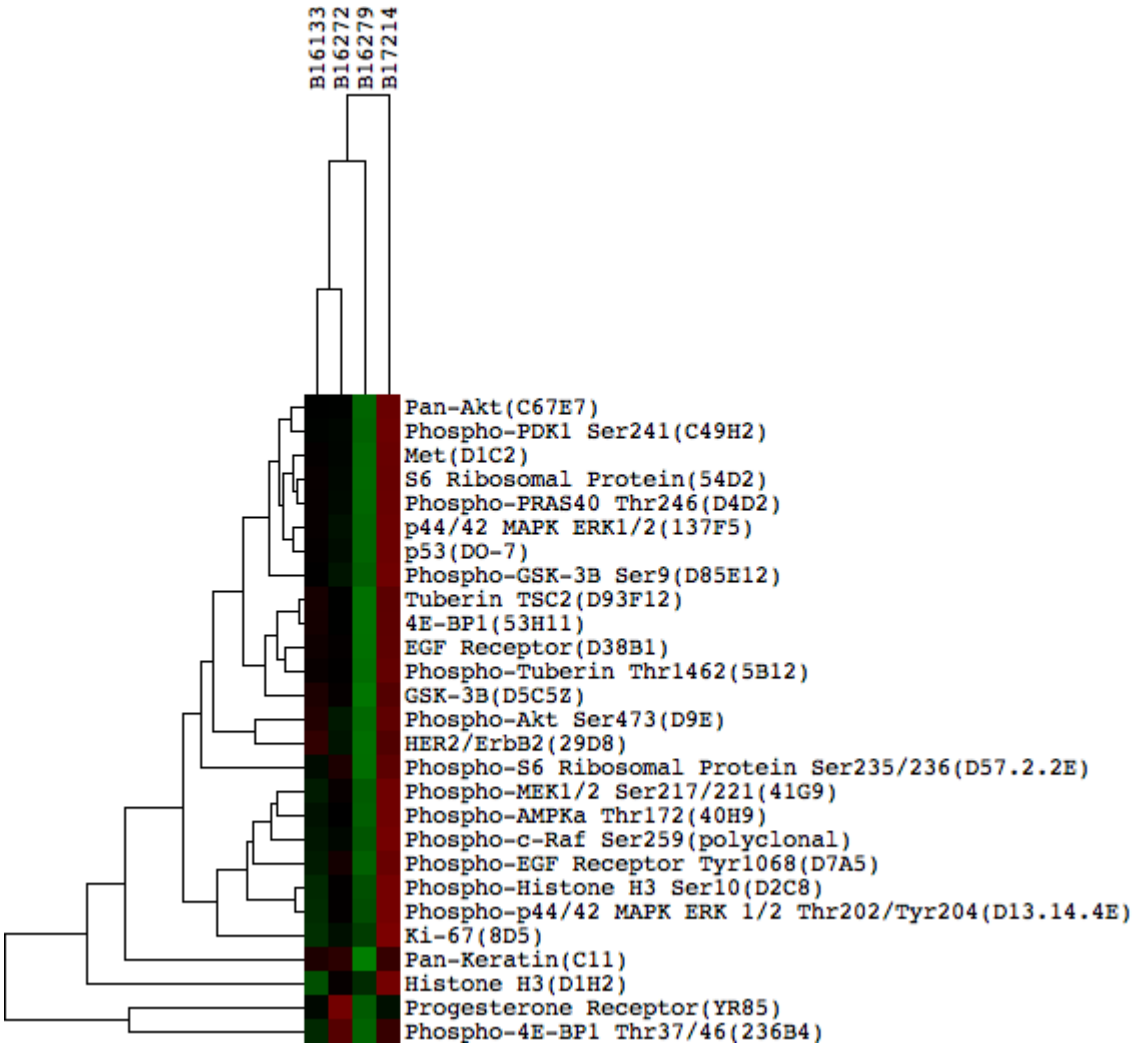

Figure (1) shows the heat map of protein profiling in Endometrial carcinomas (B16133 & B16272 moderately differentiated endometroid adenocarcinama , B16279 endometroid adenocarcinoma grade 1, B17214=Poorly differentiated Clear Cell Adenocarcinoma).