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- Title Page
- Manuscript
- Tables (if any)
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The covering letter should be uploaded at the stage of the online submission process. Explain in the covering letter, why your paper should be published in MJMHS

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The title page should be **an individual document, uploaded separately**, that provides:

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- Recommended international non-proprietary name (rINN) is required

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- Use the form of references adopted by the US National Library of Medicine and used in the Index Medicus. Use the style of the examples cited at the end of this section.
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- For a chapter or section of a book, cite the editors, authors and title of the section, and the page numbers (http://www.ncbi.nlm.nih.gov/books/NBK7271/#A34171)
- For online material, please cite the URL, together with the date you accessed the website
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Abul A, Lichtman A, Pillai S. Cellular and molecular immunology. 7th ed. Philadelphia: Elsevier Saunders; 2012.

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More than 6 authors/editors (Book, Chapter in a book & etc.)
3. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. Harrison's Principles of Internal Medicine. 17th ed. New York: McGraw Hill; 2008.

Chapter in a book
4. Vidyadaran S, Ramasamy R, Seow HF. Stem cells and cancer stem cells: Therapeutic Applications in Disease and Injury. In: Hayat MA, editor. New York: Springer; 2012.

Corporate/Organization as Author
5. Canadian Dental Hygienists Association. Dental hygiene: definition and scope. Ottawa: Canadian Dental Hygienists Association; 1995.

E-book
6. Frank SA. Immunology and Evolution of Infectious Disease [Internet]. Princeton: Princeton University Press; 2002 [cited 2014 December 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK2394/pdf/TOC.pdf

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Acknowledgements
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The format for the text varies depending on the type of article. The list of article types and their respective formats are as follows: Original Article, Review Article, Case Report, Commentary and Letters to Editors.

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- An original article is a report on the clinical objectives and analytical process, as well as a discussion of the implications of the results of a study
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  - Methods
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  - Discussion
  - Acknowledgement
  - References
  - Legends
- **The original article should not exceed 6000-word count, 4-7 figures/table and 50 references.**

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- Letters to the Editor should either offer objective and constructive criticism of published articles or discuss matters of general scientific or medical interest to readers of MJMHS.
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  - 1 small table or figure (optional)
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CONTACT

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Putra Cancer Research Symposium 2017
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ORAL PRESENTATIONS

POSTER PRESENTATIONS

Oral Presentation

Ampelopsin E Induced G2/M Cell Cycle Arrest and Apoptosis via p53-Independent Pathway in Triple Negative MDA-MB-231 Cells

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ABSTRACT

Introduction: Cancer remains as one of the most dreaded health problems worldwide. The incidence of cancer is alarming. In 2012 alone, approximately 14 million cancer cases were reported across the globe. Even with advancement in the treatment modalities such as chemotherapy, immunotherapy and radiotherapy, the survival rate of cancer patients remains poor. The issue is not only limited to some of the unbearable side effects, but drug resistance phenomenon makes cancer treatment become more challenging. For breast cancer, in particular, metastasis is the main death leading factor. Our research group explores the potential cures and lead compounds for cancer from natural products especially plants. Indeed, plants have already been a good source for a few commercially available anticancer drugs such as vindesine and taxol. Our plant of interest is *Dryobalanops* species or locally known as Kapur, which is a rich source of resveratrol oligomers (RO). In previous reports, RO have shown great potential for cancer prevention and treatment. **Methods**: Seven RO from *Dryobalanops* species (Ampelopsin E, Ampelopsin F, Flexuosol A, Laenifonol, Malaysianol A, Malaysianol D and Nepalensinol E) have been screened for cytotoxicity towards several cancer cell lines inclusive of breast cancer (MDA-MB-231 and MCF-7), colon cancer (HT29), lung cancer (A-549) and cervical cancer (HeLa). **Results**: Ampelosin E was found to be the most cytotoxic towards the triple negative cells, MDA-MB-231, among others, with the IC50 of 14.5 ± 0.71 μg/mL. Further analysis was then carried out on this compound on the mentioned most sensitive cell line. Data indicate that Ampelopsin E induced apoptosis, the most preferred mode of cell death, that doesn't inflict inflammation, thus the healthy surrounding cells are not affected. The compound arrested the cells at G2/M phase, not allowing them to complete the whole cell cycle and finally commit suicide (apoptosis). Based on the expression level of some apoptotic- and cell cycle-related proteins, we suggest that Ampelopsin E induces apoptosis via NF-κB p53-independent/p21 and mitochondrial pathways, while the cell cycle arrest is via p-53-independent/p21 pathway. These data on the mechanisms of action underlying the anticancer properties of Ampelopsin E provide some insight on how the compound eliminates the cancer cells. **Conclusion**: In short, Ampelopsin E warrants further research on its potential to be developed into an anticancer agent for the treatment of triple negative breast cancer with high metastasis tendency.

Keywords: *Dryobalanops* species, Resveratrol oligomers, Ampelosin E, Triple negative breast cancer

Oral Presentation

Biotherapeutic Effects of Probiotic Strains Isolated from Traditional Dairy Products

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ABSTRACT

Introduction: Probiotics are microorganisms, which show beneficial health effects on hosts once consumed in sufficient amounts. Some of lactic acid bacteria (LAB) group, such as *Lactobacillus* strains are considered as probiotics because of their health benefits, have a long history of consumption in traditional fermented foods, and as natural inhabitants of healthy human gastrointestinal tracts. LAB group can be isolated and characterized from traditional dairy sources. This study aimed to isolate, identify, and biologically characterize probiotic LAB strains from Iranian traditional dairy products. **Methods:** LAB strains from traditional dairy products were isolated, identified by sequencing 16s rRNA gene, and biologically characterized. Primary assessments, including low pH and high bile salt tolerance tests and experiments on antagonistic activity against pathogens and antibiotic susceptibility, verified the probiotic property of strains. The secreted metabolites from the strains and Taxol, as an anti-cancer drug, were analyzed through MTT assay to investigate their cytotoxicity in different cancer (MCF-7, HeLa, HT29, and AGS) and normal human (HUVEC) cell lines. **Results**: Results revealed the anticancer characteristics of the secreted metabolites from one of the LAB strain, *E. durans* 39C, against all cancer cell lines, similar to Taxol. The metabolites did not exhibit cell toxicity in the normal cell line. Fluorescent microscopy and flow cytometry confirmed that apoptosis is the main cytotoxic mechanism of *E. durans* 39C secretion metabolites. **Conclusion:** Newly isolated strains of LAB from traditional dairy sources can be introduced as novel candidate probiotics that could be used directly used in food industry.

Keywords: Probiotic, Traditional Dairy Food, Biotherapeutic Effect, Cytotoxicity

Oral Presentation

Exploring Canine Cancer for Comparative Research at Faculty of Veterinary Medicine, UPM

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ABSTRACT

Introduction: Many cancers in dogs and people are similar—offering opportunities for pet dogs to participate in clinical trials of treatments that could be translated to people. Fact is, several cancers in dogs are almost indistinguishable from their human counterparts, including some types of lymphoma, melanoma, breast, bone and brain cancer. Dogs are more realistic models of cancer than the rodents traditionally used in cancer research. The growing interest in dogs reflects researchers' frustration with the standard approach to developing cancer treatments: testing them in lab animals, especially mice. Mice don't normally get cancer — it must be induced — and the immune systems in many strains of lab mice have been altered. On the other hand, dogs and cats develop cancer naturally, just as people do, and have intact immune systems that plays an important role in understanding the complexity nature of cancer pathogenesis and response to therapies similar in humans. The sequencing of the dog genome in 2005 increased interest in comparative studies. The dog and human versions of that cancer involve many of the same genes and are biologically similar. Some comparative-oncology studies use cats for cancers such as oral malignancies and breast cancer, which have similarities to the human versions. But cats are used less frequently in studies than dogs, researchers say, because less is known about their tumours and cats tend to get more stressed when planning of any experimental research involving new therapies. In the recent years, there has been increased number of cancer cases in dogs presented to the University Veterinary Hospital (UVH) of Faculty of Veterinary Medicine in Universiti Putra Malaysia (UPM) with skin cancer being the most common; oral, mammary cancer, lymphoma, bone and bladder cancer. Cancer in dogs are routinely diagnosed and staged using several diagnostic approaches including radiography, computed tomography, endoscopy, magnetic resonance imaging (MRI), and ultrasonography; cytology; histopathology and blood tests. Currently, cancer in pet animals are treated through surgical interventions, chemotherapy, tyrosine kinase inhibitors and advanced immunotherapeutic vaccines. Humane euthanasia is recommended for those dogs with advanced stages of cancer. UPM veterinary clinical researchers have begun recruiting dogs with spontaneous cancers for research on cancer stem cells, molecular pathogenesis, biomarkers and trials on new therapies including novel drug delivery methods and palliative medicine. These efforts are made possible through collaboration between the medical and veterinary faculty members; and the UVH where the dogs with cancer is presented for treatment. Research on spontaneous cancer in dogs requires approval from the Institutional Animal Care and Use Committee (IACUC) of UPM and consent from the UVH management and pet owners. **Conclusion:** It is of hope that the ongoing research on dogs with spontaneous cancer in Malaysia can improve the survival and outcome of dogs with cancer; and indirectly the new therapies evaluated in dogs can next be translated to the human bedside in future.

Keywords: Canine cancer, Comparative oncology, Clinical trial, Therapies, Malaysia

Oral Presentation

Cancer Stem Cells: Opportunities and Challenges in Cancer Research

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ABSTRACT

Introduction: Cancer stem cells (CSCs) is a subset of cancer cells that has the ability to self-renew and differentiate into other cancer cells. Residual CSCs that are incompletely removed by surgery have been shown to cause cancer recurrence. Due to the increase expression of chemical efflux pumps, CSCs are more chemical resistant and therefore are more resistant towards chemotherapy and may contribute to cancer relapse. Therefore, there is ever increasing efforts in understanding CSCs as a therapeutic target. One of the main challenges in studying CSCs lies in the difficulty in isolating CSCs. **Methods:** In our lab, we cultured bladder cancer cell lines in ultra-low attachment tissue culture plates with media that contained various growth factors. **Results:** Under these conditions, putative CSCs grew as spheroids. The next challenge in CSCs research is the identification of CSCs. Cell surface markers, in combination with gene expression studies and serial-dilution assay have been used to further identify. Our lab has used gene expression study to show that putative bladder CSCs expressed high levels of genes commonly associated with regular stem cells as well as Notch signalling genes. Next, we showed that a small molecule inhibitor, which is being investigated as a therapeutic entity, can affect the growth of bladder CSCs. **Conclusion:** Our study demonstrates that putative bladder CSCs could be cultured from cell lines. Further studies are needed to affirm the identity of these cells. These cells will be used in the future as a model to study the biology of CSCs as well as explore the potential use of small molecules that target these cells specifically.

Keywords: Cancer stem cells, Notch signalling, Bladder cancer, Small molecules

Oral Presentation

Clinico-pathological Alterations of *N*-methyl-*N*-nitrosourea-induced Leukaemia-Lymphoma in Rats.

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ABSTRACT

Introduction: Intraperitoneal exposure of *n*-methyl-*n*-nitrosourea (MNU) induces development of leukaemia-lymphoma in rats. There is no study reported on development of leukaemia-lymphoma in rats through oral MNU exposure. Hence, the study aims to compare the clinico-pathological changes of MNU-induced leukaemia-lymphoma rats through intraperitoneal and oral exposures. **Methods:** Sprague Dawley rats were divided into control, oral-MNU, and intraperitoneal (IP)-MNU group (n=9). Both MNU groups received four injections of MNU at 60 mg/kg body weight per administration in two weeks period. Blood samples were collected and total white blood cell (WBC) counts were determined using an automated haematology analyser. Blood smears were prepared and stained with Wright's staining for differential WBC counts. Presence of immature cells were included in the differential count of 100 cells. Serum biochemistry analysis was performed for liver, kidney and muscle parameters. Histopathology examination of spleen, mesenteric lymph nodes, liver, lungs, kidneys and heart were performed for the evaluation of leukaemia-lymphoma metastasis. **Results:** Results showed IP-MNU group had high percentage of accelerated-phase of chronic myeloid leukaemia (CML) and low percentage of blast-phase of CML, while oral-MNU group only had accelerated-phase of CML. On the other hand, regardless of route of MNU exposures, splenic and nodal lymphoma were observed in all rats administered with the carcinogen. All selected vital organs showed evidences of metastatic lymphoma-leukaemic cells with higher percentages observed in the heart (89%) and lungs (100%) of IP-MNU group. Meanwhile there were no remarkable alterations in the serum biochemistry of all MNU-induced rats. **Conclusion:** This study suggested that exposure of MNU in rats via IP route induces CML accelerated- and blast-phase with higher incidences of pulmonary and cardiac lymphoma metastasis compared to oral route.

Keywords: Chronic myeloid leukaemia, Lymphoma, Metastasis

Oral Presentation

Depression among Breast Cancer Patients

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ABSTRACT

Introduction: Breast cancer is one of the most feared diseases among women, and depression is one of the most common psychiatric disorders encountered in breast cancer patients. Breast cancer patients may experience depression at any stage of their illness; from initial diagnosis to the terminal phase of the illness. Studies in Western countries have shown that the prevalence of depression ranges from 1 % to 56 %, whereas the prevalence of depression from Asian studies was between 12.5 % and 31.0 %. Factors associated with depression in breast cancer patients include socio-demographic factors, cancer-related factors, treatment-related factors, other psychological factors, lifestyle, social support, and quality of life. **Conclusion:** There are simple coping strategies to help these patients such as social support, teaching them to accept their condition and interpreting it positively, spiritual support, and providing support at work.

Keywords: Breast cancer, Depression, Prevalence, Associated-factors, Coping strategies

Oral Presentation

Development of Nanomedicine in Preclinical Cancer Research: To Deliver on a Promise

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ABSTRACT

Introduction: Battling cancer has been an excruciating fight, moving unbearably slowly and some battles are far from realising success. Often there are many casualties along the way. The clinical management of cancer has enjoyed development in the past decade, where there has been some improvement in clearance rates of cancer cases, better prognosis and enhanced survival times. In continuing with battling against cancer, nanotechnology has gained significant attention in recent years when the technology enables the delivery of therapeutic agents to be greatly improved, specifically targeting the disease cells which allow better diagnosis and treatment of cancer at the cellular level. The main goal of drug delivery system is to achieve desired concentration of drug in the blood or specific target tissue, which is therapeutically effective and non-toxic to healthy cells for a required period. **Methods:** In our research work we have attempted to synthesize effective nanomaterials with bioactive natural compounds with less toxicity towards healthy cells, which were then further tested to observe deposition of the nanomaterials in selected *in vitro* and *in vivo* model. **Results**: The developed nanomedicine was tested on cancer induced liver mouse model and observation made will be further described and discussed to furnish the evidence showing satisfactory delivery of nanomedicine to specific target cells. **Conclusion:** Thus, this may be a promising development in drug nanodelivery system.

Keywords: Nanomedicine, Bioactive natural compounds, Nanodelivery system

Oral Presentation

Glucosinolates and their Hydrolysis Products are Potent Inducers of Apoptosis and Cytotoxicity in Various Cancer Cells

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ABSTRACT

Introduction: Epidemiological studies have shown that the consumption of cruciferous vegetables is associated with reduced risk of various types of cancer. Glucosinolates, which are present in large quantities in radish and other cruciferous vegetables, are hydrolysed by myrosinase to form isothiocyanates, which are believed to be responsible for chemopreventive activity; however, the underlying mechanisms of action have not been investigated, particularly in human cell lines. **Methods**: The aim of the study was to assess the cytotoxicity of isothiocyanates in various cancer cells and evaluate their potential to enhance apoptosis. The cytotoxic and apoptotic assessment of isothiocyanates were carried out ensuing an initial screening assay with various cell lines, including MCF-7, MDA-MB-231, HT-29, and HepG2. Isothiocyanates displayed cytotoxicity in the cells following incubation for 24, 48 and 72 hours respectively, in comparison to a positive control. In contrast, the intact glucosinolates showed no cytotoxicity. **Results:** Morphological studies indicated that isothiocyanates stimulated apoptosis as exemplified by cell shrinkage, blebbing, chromatin condensation, and nuclear fragmentation. The Annexin V assay revealed significant increases in apoptosis for both the early and late apoptotic stages. Finally, impairment of cell proliferation was indicated by cell cycle arrest phase as compared to the control. **Conclusion:** It may be concluded that isothiocyanates, but not their parent glucosinolates, stimulate apoptosis and cause cytotoxicity in cancer cells.

Keywords: Glucosinolates, isothiocyanates, Apoptosis, Cytotoxicity, Cancer cells

Oral Presentation

In vitro Cytotoxic Activity of Extracts from *Barrientosiimonas humi* on Cancer Cell Lines

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ABSTRACT

Introduction: *Barrientosiimonas humi* (*B. humi*) is a novel genus of phylum *Actinobacteria* and first discovered in Antarctica, a pristine continent on Earth with extreme and harsh environment that limited survival of microorganisms, by Assoc. Prof. Dr. Cheah Yoke Kqueen and team in 2011 during XI Ecuadorian Antarctic Expedition (2007). *Actinobacteria* are known as the most prolific producers of numerous natural products with diverse biological activities associated with medicinal value such as antibiotic, anti-tumor, anti-cancer, and anti-infection. To date, this is the first report of antibacterial and anticancer activities exhibited by members of the family *Dermacoccaceae* under the phylum *Actinobacteria*. Most of the commercially available chemotherapeutic drugs such as bleomycin, daunorubicin and doxorubicin are isolated from soil *Actinobacteria*. Currently, searching for new and effective chemotherapeutic agents is an urgent medical need due to the problems of systemic toxicity and multidrug resistance in cancer. Preliminary screening of the crude extract of *B. humi* showed significant antimicrobial and anticancer activities. Therefore, the aim of this study was to evaluate the cytotoxicity effects of the bioactive compounds produced by *B. humi* on various cancer cell lines. **Methods**: The bioactive fractions were derived from the ethyl acetate extracts of *B. humi*. Cell lines tested were Human breast cancer cell lines (MCF-7 and MDA-MD- 231), colon cancer cell line (HT-29), liver cancer cell line (HepG2), lung cancer cell line (A549), prostate cancer cell line (PC-3) and tongue cancer cell line (SCC-9). Cytotoxicity screening using 3-(4,5- dimethylthiazol-2-yl)-2,5-diphenyltetrazholium bromide (MTT) assay was confirmed using a Real Time Cellular Analysis (RTCA) system, a label-free assay for real time monitoring of cell viability. Toxicity assessment was conducted on embryonic heart normal cell line (H9c2). Doxorubicin was used as positive control and DMSO as solvent control. Bioassay-guided fractionation using chromatography was applied to help resolve and narrow the search of bioactive compounds. The crude ethyl acetate extract of *B. humi* inhibited cell growth of both human breast cancer cell lines in dose and time dependent manner. Data were analyzed using GraphPad Prism 5.0 and one-way ANOVA, at significance level $P < 0.05$. **Results**: Two out of four fractions showed significant cytotoxicity activity on human breast cancer cells. All fractions were found to be non-toxic to the normal cell lines. Hence, the active fraction was selected for apoptosis analysis. Drug treated breast cancer cells resulted in higher population of early and late apoptotic population compared to control. Furthermore, phenotypic microarray was used to characterize metabolic phenotypes of treated cancer cells to further understand the pathway involved by the *B. humi* fraction. **Conclusion:** Potential bioactive fractions derived from *B. humi* were successfully identified and characterized. Further investigation of other experimental studies may confirm that these potential leads could make impact and help to accelerate the pipeline of anticancer drug discovery.

Keywords: *Barrientosiimonas humi,* Cytotoxic, Bioactive Fractions, MCF-7, MDA-MB-231

Oral Presentation

Leukaemia Stem Cells in Acute Myeloid Leukaemia

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ABSTRACT

Introduction: Leukaemia is a cancer of white blood cells. It is diagnosed in approximately 352,000 people every year (2% of total cancers) and kills 265,000 worldwide. In Malaysia (2007-2011), leukaemia is the sixth most common cancer with incidence rates of 4.2 and 3.4 per 100,000 in males and females, respectively. Two main lineages are lymphoid and myeloid leukaemia. The Malaysian National Registry reports an average of 266 new cases of myeloid leukaemia in males and 230 cases in females each year. Acute myeloid leukaemia (AML) are transformed immature myeloid cells in the bone marrow. It is a heterogeneous disease that is aggressive and difficult to treat. A Swedish article reported early death in 19% of patients. With intensive chemotherapy, 65% achieve complete remission. Overall survival for the younger age group (16-55 yo) is 7 years while in the older age (76-89 yo) is only 0.5 years. Leukaemia stem cell is associated with early relapse in AML and poor survival. Its clinical significance is hampered by the unavailability of suitable identity markers. Objective: To determine AML samples with stem cell like features and identify highly expressed genes. **Methods**: Cell culture and MTS assay were used to differentiate samples with high *in vitro* growth. Subtractive hybridization was conducted to isolate a library of highly expressed genes while cloning, colony PCR and DNA sequencing was performed to identify the genes. **Results**: AML samples with high proliferative potential (PP) was inversely correlated with patient's duration of disease free survival (DFS). Genes isolated from one of these samples showed many stem cell associated features. **Conclusion**: These genes are potential markers to identify leukaemia stem cells in AML and should be validated on a larger number of samples.

Keywords: *In vitro* proliferation, Disease free survival, Embryonic genes, Oxidative respiratory genes

Oral Presentation

Nanotechnology for the Improvement of Biomedical Research (Cancer Research)

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ABSTRACT

Introduction: This paper presents design, synthesis, and characterization, as well as the applications of nanomaterials biomedical research, focusing on the efficient delivery of anticancer drug tamoxifen and intracellular delivery of siRNA across biological barriers to target cells. This can be achieved by the synthesis of polymeric drug delivery system of encapsulated tamoxifen citrate (TAM) and MNPs for breast cancer treatment. For siRNA delivery, magnetic properties of super paramagnetic iron oxide (SPIO) nanoparticles enable it to package siRNA into nanoparticles for it to enter the cancerous cell membrane easily. Introducing targeted drug and gene delivery system will increase tissue selectivity and improve its toxicity profiles **Methods**: Iron oxide was synthesized via co-precipitation method and coated with oleic acid at 80^0C to improve the stability of the superparamagnetic iron oxide nanoparticles (SPIO). Tamoxifen citrate (TAM) and siRNA were conjugated with nanomaterials that consist of superparamagnetic iron oxide nanoparticles (SPIO) and quantum dots (QD) to enhance intracellular delivery across biological barriers and cellular uptake by targeted cells, breast cancer cell line and lung cancer cell lines, respectively. The functionalized nanoparticles were characterized and analysed using X-ray Diffraction Analysis (XRD), Energy-dispersive X-ray spectroscopy (EDXRF), vibrating sample magnetism (VSM) and transmission electron micrograph (TEM). Conjugated tamoxifen citrate (TAM) and siRNA with nanomaterials were tested for their colloidal stability, drug release and nanotoxicity. **Results:** Magnetic nanoparticles (SPIO) possess the ability to deliver targeted anticancer drug, tamoxifen as well as can package gene (siRNA) into the nanoparticles for targeted gene delivery. **Conclusion:** We successfully encapsulated TAM and SPIO together to improve the treatment for breast cancer while the incorporation of SPIO nanoparticles and QD in the siRNA delivery will help to provide efficient, multifunctional and nontoxic siRNA delivery agents for lung cancer therapy.

Keywords: Nanomaterials, Drug delivery, Gene therapy, siRNA, SPIO

Oral Presentation

Oncolytic Recombinant Newcastle Disease Virus for the Treatment of Cancer: Current and Future Prospects

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ABSTRACT

Introduction: Newcastle disease virus (NDV) is an economically important avian paramyxovirus type I that causes substantial loss to the poultry industry worldwide. Although the virus does not cause any major infection in humans it specifically multiplies in and kills human cancer cells, giving it a huge potential to be developed as an oncolytic therapeutic vaccine. The first report of using NDV for acute leukaemia was published in 1964. In the following year, Cassel and Garrett published a more comprehensive study on NDV as an antineoplastic agent. Since then, a lot of research has been done on oncolytic NDV. Early findings focussed on selecting natural occurring NDV strains and determining their potential in killing cancer cells *in vitro* and *in vivo*. The mechanism of NDV-induced cell killing in cancer cells that are hypoxic, interferon-resistant, apoptosis-resistant, and immunotherapy-resistant has been the central focus in many laboratories. With advances in genetic engineering and reverse genetics, recombinant NDVs expressing immunomodulatory and pro-apoptotic transgenes were produced to enhance the viral oncolysis. **Methods:** Parallel to that, the post oncolytic anti-tumour immunity was investigated with the aim of developing viral oncolysates as vaccines for post-operative management of melanoma cancer. The viral oncolysates were prepared by harvesting the cancer cells from the patients or similar cancer cell lines which were then infected with NDV. The infected cancer cells were then lysed by sonication before the lysates were collected for treatment. The vaccinations were performed over many years and reports from 10- and 15-year follow-ups showed prolonged survival of many patients from 33% of the unvaccinated control to more than 63% and 55% of the vaccinated group, respectively. In the 1980s, another vaccine called autologous tumour cell vaccine modified by infection with NDV (ATV-NDV) was developed. Unlike the oncolysates, the infected cancer cells remain viable prior to be used as a vaccine. The vaccine was shown to augment tumour-specific cytotoxic T cell (CTL) and tumour-specific T helper responses in mice. Clinical trials showed significantly improved overall survival in cancer patients. Despite these promising results from clinical trials, cancer patients have not fully benefited from oncovirotherapy, due to scepticism and resistance from clinicians and the public. With better understanding of virotherapy, a combinatorial treatment using physical, immune cells and/or virus therapies could be a way forward. Two reported case studies using local hyperthermia, NDV and dendritic cells vaccination prolonged the survival of a bone-metastases prostate cancer and a liver-metastases breast cancer patient. **Conclusion:** This treatment modality could be a lifesaving option for other cancer patients soon.

Keywords: Newcastle disease virus, Cancer vaccine, Oncolysis, Tumour immunity, Virotherapy

Oral Presentation

Relevance of Aberrations in Signal Transduction Pathways and Tumour Microenvironment in Colorectal Cancer for Cancer Precision Medicine

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ABSTRACT

Introduction: Cancer precision medicine is aimed for selecting treatments targeted to the needs of the individual patients based on the biomarker, genetic or phenotypic characteristics of the cancer cells. The ultimate aim is to improve clinical outcome and to minimize side effects. Current targeted therapies have arisen from decades of research on signal transduction pathways and major discoveries in immunology (*Seow et al., OncoTargets and Therapy 2016,9: 2565-2574*). It is well-documented that signalling pathways such as phosphoinositide 3-kinase (PI3K) and WNT are frequently deregulated pathways in several human cancers, including CRC and blockade of these pathways could potentially be useful for cancer therapy. One of the targeted drugs approved for metastatic colorectal cancer patients with wild type KRAS is cetuximab which targets the epidermal growth receptor (EGFR). *KRAS* mutations have been shown to be negative predictors of response to cetuximab. *RAS* and *BRAF* can acquire activating mutations, which render EGFR inhibitors ineffective. **Methods**: Thus, there is a need to screen for RAS and BRAF mutations before starting anti-EGFR therapy. One of the objectives of this talk is to provide an insight into the incidence of *RAS*, *BRAF*, *PI3K* and *pTEN* mutations (*Yip WK et al., Acta Pathol Microbiol Immunol Scand (APMIS), 2013, 121: 954-66*). **Results:** In addition, we have also determined the relationship between biomolecules of the WNT and Notch signalling pathways by immunohistochemical staining, the effects of small chemical inhibitors and antisense strategies by using inhibitors of microRNAs on cancer cell growth and angiogenesis. The tumour microenvironment can influence tumour growth and progression, and metastasis. The phenotypes of macrophage in primary CRC can be detected by immunohistochemistry and molecular interactions following interaction between M1 and M2-like macrophages and cancer stem-like cells are currently under investigation. **Conclusion:** These approaches provide insights into the molecular alterations in cancer and may assist in the development of new strategies for treatment of cancer.

Keywords: Signal transduction, Precision medicine, KRAS, M2 macrophages, Cancer stem cells

Oral Presentation

Role of Human Papillomavirus (HPV), Estrogen and Apobec3B Axis in Breast Cancer Initation

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ABSTRACT

Introduction: Human papillomaviruses (HPVs) are known to cause cancer by altering multiple signaling pathways through integration of their oncogenes into the human host genome. It has been well established that infection with HPVs causes cervical cancer and head and neck cancer; and some forms of genital cancers. The HPV viral oncogenes E6 and E7 play a big role in carcinogenesis. HPV E6 proteins bind to p53 to inhibit and degrade this tumour suppressor to abolish its cancer prevention effects. Consequences of an inactivated p53 also include accumulation of gene mutations and inappropriate response to DNA damage, which co-operate with other cellular changes, eventually leading to carcinogenesis. The APOBEC (apolipoprotein B editing enzyme catalytic polypeptide-like) proteins function in innate immunity by deaminating single-stranded DNA (ssDNA) replication intermediates of viral pathogens (retro-, hepadna-, papilloma-viruses), inhibiting the retrotransposition of L1 and Alu elements and mediating the clearance of foreign DNA through deamination-dependent mechanisms. APOBEC enzymes have also been implicated in cancer pathogenesis. In HPV-positive cancers of the head/neck and cervix, the HPV E6/E7 oncoprotein causes upregulation of APOBEC3B both at the mRNA and enzymatic activity level. **Methods:** As such, we decided to investigate the prevalence of HPV in breast cancer and whether APOBEC3B is overexpressed in breast cancer samples. **Results:** Detection of HPV DNA via the Toshiba DNA chip platform technology found 31% of breast cancer samples were positive for high-risk HPV especially HPV16 and HPV18. HPV prevalence was significantly correlated with estrogen receptor, pathological features of the cancer, and age of patients. A significantly higher proportion of ER-positive BC samples were HPV-positive than ER-negative samples. Interestingly, HPV-positive tumors showed better prognosis than HPV-negative tumors. Our *in vitro* study of normal breast epithelial cells transfected with HPV18 showed enhanced apobec3B expression, which led to γH2AX focus formation, a classic sign of genomic instability, and DNA degradation. These A3B induction effects were abrogated when E6, E7 and A3B gene expression was knocked down using shRNA. Finally, we also checked if A3B induction is correlated with HPV status in breast cancer patients. A3B expression level seems to be correlated with HPV infection although statistical significance could not be obtained. In summary, we propose a putative mechanism of breast cancer development whereby Apobec3B induction due to HPV infection in mostly estrogen-receptor positive cells leads to aberrant DNA mutations that initiate carcinogenesis. **Conclusion:** Indeed, it is highly likely that a synergy between estrogen and p53 insufficiency caused by HPV E6 oncoprotein induces Apobec3B expression which leads to initiation of breast carcinogenesis.

Keywords: Breast cancer, Human papillomavirus, Estrogen receptor

Oral Presentation

Searching for Universal Cancer Biomarkers in Micronutrients with Mathematics

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ABSTRACT

Introduction: Currently, there is little known about the coordinated regulation of the plethora of micronutrients involved in biochemical pathways. For example, iron is an essential micronutrient that is an absolute requirement for correct cellular function in all eukaryotic organisms. Yet ferrous iron can also catalyse the formation of potentially toxic reactive oxygen species, such as hydroxyl radical via the Fenton reaction, and regulation of iron metabolism is therefore of critical importance. Dysregulation of iron metabolism in cancer is well known, and it has been argued for years that excess iron and increased cancer incidence occur simultaneously. Link between excess iron and cancer in many studies are suggested by the efficacy of iron deprivation and iron chelators in cancer therapy. It was also observed that levels of transferrin receptor 1 (TfR1) are elevated in cancer, and use of TfR1 as a targeting ligand in the design of anti-cancer was proposed. **Methods:** This work utilizes module preservation statistics for determining which properties of a gene network module are preserved in a second (test) network. The module preservation statistics allow one to quantify which aspects of within-module topology are preserved between a reference gene network and a test gene networks. This work uses breast cancer microarray data (as a reference network) and prostate cancer/healthy breast/healthy prostate microarray data (as test network) to determine whether human liver iron metabolism gene network is preserved in both cancer cells but not in healthy cells. For the measurement of similarity one statistical benchmark was used: $Z_{summary}$. **Results:** Since human liver iron metabolism gene network is not defined via a clustering procedure, it is not clear whether cluster preservation statistics are appropriate for analysing this example. Thus, module preservation statistics were used instead. In the module preservation statistics: If $Z_{summary}>10$, there is strong evidence that the module is preserved; if $2<Z_{summary}< 10$, there is weak to moderate evidence of preservation; if $Z_{summary}< 2$, there is no evidence that the module preserved. Overall, this research found strong evidence of iron metabolism gene network preservation ($Z_{summary}>10$) in the breast cancer and prostate cancer but no evidence ($Z_{summary}<2$) of iron metabolism gene network preservation in breast cancer and healthy breast/prostate. This work found that the connectivity of the breast cancer iron metabolism gene network is most strongly preserved in the prostate cancer iron metabolism gene network. **Conclusion:** The presence study suggested that iron can be a universal cancer biomarker because the strong evidence of iron metabolism gene network preservation in breast cancer and prostate cancer.

Keywords: Cancer biomarker, Transferrin receptor I, Module preservation statistics, Iron metabolism

Oral Presentation

Synthesis and Characterization of Tin (Iv) Dithiocarbazate Complexes and Their Anticancer Properties

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ABSTRACT

Introduction: There has been a marked growth in the research of metal-containing complexes as anticancer agents over the past few decades that was triggered by the discovery of cisplatin in cancer treatment. Cisplatin was later found to produce toxic effects and subsequently, cancer cells developed resistance towards cisplatin, rendering it to be less effective. Thus, non-platinum based complexes have been developed to be used in cancer therapy, among which tin(IV) complexes have gained importance due to their activities against a wide spectrum of cancers as well as their reduced toxicity compared to platinum-based complexes. **Methods:** Three novel tin complexes were synthesised from the condensation reaction of tin(IV) chloride, diphenyltin(IV) dichloride and dimethyltin(IV) dichloride with S-2-methylbenzyl-β-N-(2-hydroxy-3-methoxybenzylene) dithiocarbazate (S2MOVaH) derived from S-2-methylbenzyl dithiocarbazate and 2-hydroxy-3-methoxybenzaldehyde via reflux. S2MOVaH and the tin complexes were characterised using elemental analysis, FTIR, molar conductivity, GCMS, UV-Vis, FTIR, ^{1}H, ^{13}C, and ^{119}Sn NMR spectral studies. **Results:** The complexes were non-electrolytes in DMSO, where anionic S2MOVaH was bonded covalently to the metal ions with 1:1 molar ratio. The infrared spectral data showed that the chelation behaviour of the tridentate binegatively-charged S2MOVaH Schiff base towards tin ions was through the thiolo sulphur, azo nitrogen, and phenolic oxygen. The electronic spectral results indicated the existence of $\pi \rightarrow \pi^*$ (phenyl rings) and $n \rightarrow \pi^*$ (─N═N). The trigonal bipyramidal molecular structure of $Sn(S2MOVa)Me_2$ was determined using X-ray crystallography. Molecular docking was used to predict the binding between the tin complexes and the receptors of ribonucleotide reductase (pdb ID: 4R1R), thymidylate synthase (pdb ID: 2G8D), and thymidylate phosphorylase (pdb ID: 1BRW) enzymes. In addition, the anticancer activities of the tin complexes were investigated against bladder cancer (RT-112 and EJ-28) cell lines and the organotin complex was markedly more cytotoxic than the S2MOVa Schiff base. **Conclusion:** This study has shown that tin complexes are promising anticancer agents, and slight changes in the structures of the complexes produced complexes that had varying activities against the cell lines tested.

Keywords: Dithiocarbazate, Schiff bases, Tin(IV) complexes, Anticancer activities, Bladder cancer cells

Oral Presentation

Tobacco Control Policies and Public Health

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ABSTRACT

Introduction: Tobacco tax is the most effective measure to reduce smoking attributable mortality and morbidity. The higher price reduces the prevalence of tobacco use and consumption of tobacco products. In 2008, WHO-FCTC provides evidence based guidance for countries to improve their national tobacco control policies known as MPOWER which includes taxation and other non-price policies. **Methods:** Malaysia Abridged SimSmoke, a simulation model is developed to estimate the impact of tobacco taxation and other non-price policies on smoking prevalence, number of reduction in smokers and the associated smoking attributable deaths in short, medium and long term. Using the specific policy parameters, the model incorporated the most recent smoking prevalence and population size for Malaysia. **Results:** The increase of cigarettes excise tax from 42.03% to 49.4% of retail price in November 2015 is expected to decrease smoking prevalence to 21.8% in the short term (within 5 years) and 20.7% in the long run (in 40 years). This reduction will result in 473,472 fewer smokers and will reduce smoking attributable deaths by 236,736 or by 8.8% in 40 years. However, if the excise tax is further increase from 49.4 % to 70% of retail price as suggested by WHO, the current smoking prevalence is estimated to decrease from 22.8% to 18.8%, 16.8% and 14.8% in short, medium and long term, respectively. Overall, the tax increase will reduce around 1.85 million number of smokers and it is predicted to avert 926,534 deaths within the next 40 years. If the increase in excise tax is accompanied by bans in all forms of advertising/promotion, implements and enforcement of comprehensive smoke-free policies and runs intensive mass media campaigns on the harmfulness of tobacco, around 2.4 million and prevent 1.2 million smoking-attributable premature deaths would be reduced in long term. **Conclusion:** The model predicts that many premature deaths can be averted by increasing tobacco excise tax. Government should increase the excise tax not less than the suggested 70% of retail price to have a greater impact on the smoking prevalence and smoking attributable death. Indeed, to elevate the effectiveness of the tobacco control policies, the taxation policy must be strengthened with other combined non-price policies.

Keywords: Tobacco, Smoking, Prevalence, Taxes, Premature, Taxes

Oral Presentation

Unequivocal Ultrastructural Degenerative Changes as Evidences of Apoptosis

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ABSTRACT

Introduction: In view of the absence of clear-cut equivalence between ultrastructural alterations and biochemical cell death characteristics, the *Nomenclature Committee on Cell Death* (NCCD) decided that the "official" classification of cell death modalities had to rely purely on morphological criteria (Galluzi *et al*. 2007). With reference to the above current reports on the occurrence of apoptosis in investigations on the search for the treatment of cancer were supported by limited evidences of ultrastructural degenerative changes *viz.* cytoplasmic blebbing and nuclear fragmentation; the latter in most cases were dubious and unconvincing. More alarming cellular degenerative changes characteristic of necrosis were identified as apoptosis. To demonstrate the occurrence of apoptosis there must be a sequence of nuclear degenerative changes evidenced by peripheral nuclear chromatin condensation, nuclear lobulation, nuclear fragmentation (apoptotic body) and phagocytosis of apoptotic bodies. Phagocytosis is an important component of apoptosis as absence of phagocytosis will lead to accumulation of apoptotic bodies which could interfere with tissue repair and regeneration. Further, current studies on the search for the treatment of cancer are primarily directed towards the occurrence of apoptosis in cancer cells. Without attention given to another and equally important component of cancer tissue which is its vasculature, studies on the search for the treatment of cancer is incomplete. This presentation deliberates the mechanism of vasculature break-down during regression of the corpus luteum to unequivocally demonstrate the sequence of degenerative changes that occur during apoptosis. The heavily vascularized, rapid development of the corpus luteum following ovulation resembles that of oncogenesis. In the absence of fertilization the corpus luteum undergo an equally rapid regression – deletion of luteal cells and capillary bed. **Conclusion:** In this respect corpus luteum development and involution is a perfect model to study the development of and successful treatment of cancer.

Keywords: Apoptosis, Sequence of nuclear degenerative changes, Vasculature break-down, Phagocytosis, Necrosis

Poster Presentation

Nanotechnology for Improvement of Biomedical Research (Cancer Research)

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ABSTRACT

Introduction: This paper presents design, synthesis, and characterization, as well as the applications of nanomaterials biomedical research, focusing on the efficient delivery of anticancer drug tamoxifen and intracellular delivery of siRNA across biological barriers to target cells. This can be achieved by the synthesis of polymeric drug delivery system of encapsulated tamoxifen citrate (TAM) and MNPs for breast cancer treatment. For siRNA delivery, magnetic properties of super paramagnetic iron oxide (SPIO) nanoparticles enable it to package siRNA into nanoparticles for it to enter the cancerous cell membrane easily. Introducing targeted drug and gene delivery system will increase tissue selectivity and improve its toxicity profiles **Methods**: Iron oxide was synthesized via co-precipitation method and coated with oleic acid at 80ºC to improve the stability of the superparamagnetic iron oxide nanoparticles (SPIO). Tamoxifen citrate (TAM) and siRNA were conjugated with nanomaterials that consist of superparamagnetic iron oxide nanoparticles (SPIO) and quantum dots (QD) to enhance intracellular delivery across biological barriers and cellular uptake by targeted cells, breast cancer cell line and lung cancer cell lines, respectively. The functionalized nanoparticles were characterized and analysed using X-ray Diffraction Analysis (XRD), Energy-dispersive X-ray spectroscopy (EDXRF), vibrating sample magnetism (VSM) and transmission electron micrograph (TEM). Conjugated tamoxifen citrate (TAM) and siRNA with nanomaterials were tested for their colloidal stability, drug release and nanotoxicity. **Results:** Magnetic nanoparticles (SPIO) possess the ability to deliver targeted anticancer drug, tamoxifen as well as can package gene (siRNA) into the nanoparticles for targeted gene delivery. **Conclusion:** We successfully encapsulated TAM and SPIO together to improve the treatment for breast cancer while the incorporation of SPIO nanoparticles and QD in the siRNA delivery will help to provide efficient, multifunctional and nontoxic siRNA delivery agents for lung cancer therapy.

Keywords: Nanomaterials, Drug delivery, Gene therapy, siRNA, SPIO

Poster Presentation

Nanomaterials-mediated siRNA Delivery System for Gene Therapy in Lung Cancer Cells

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ABSTRACT

Introduction: Gene therapy brings the new frontier in cancer treatment where new nanotechnology-based, safe and efficient delivery methods are also being developed. Double stranded RNA-mediated interference (RNAi) is a promising candidate in targeted cancer therapy in order to combat the limitations in conventional drug delivery system and adverse side effects of the chemotherapy regime. Small interfering RNA (siRNA) functions as potent therapeutic agents to induce gene silencing mechanism in RNA interference (RNAi). However, due to the limited delivery of siRNA through cell membrane, various nano-delivery systems have been developed to facilitate siRNA access to cytoplasm of the targeted cells. **Methods:** siRNA was conjugated with nanomaterials that consist of superparamagnetic iron oxide nanoparticles (SPION) and quantum dots (QD) to enhance intracellular delivery across biological barriers and cellular uptake of the targeted cells. The characterizations of synthesized nanoparticles were tested with X-Ray Diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR), Transmission Electron Microscopy (TEM), Dynamic Light Spectroscopy (DLS) and Vibrating Sample Magnetometer (VSM). **Results:** Magnetic nanoparticles (SPIO) possessed the ability to package siRNA into nanoparticles for it to enter the cancerous cell membrane easily. Semiconductor quantum dots (QDs) functions as multi-colour biological probes which helps in monitoring siRNA delivery. The fluorescent nanoparticles QD able to track delivery of nucleic acid, sort cell by degree of transfection and purify homogenously silenced subpopulations. Future study will focus on the cellular uptake and cellular internalization of nanoparticles and gene silencing activity using Ultraviolet Visible Spectroscopy (UV-VIS), Confocal Laser Microscopy (CLFM), Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) and flow cytometry. The formulation will be tested on two different cell lines, namely A549 human lung carcinoma and MRC5 human lung fibroblast cell. The toxicity test of the nanomaterials-siRNA formulations will be conducted using MTT assay. **Conclusion:** The incorporation of SPIO nanoparticles and QD in the siRNA delivery will help to provide efficient, multifunctional and nontoxic siRNA delivery agents for cancer therapy.

Keywords: Gene therapy, siRNA, Nanocarriers, SPION, Quantum dots

Poster Presentation

Anti-proliferative and Apoptosis Induction Effects of Cashew Shoot Extract in Breast Cancer Cells

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ABSTRACT

Introduction: Anacardium occidentale or also known as cashew is a popular traditional plant among Malaysian community. The shoots of this plant is commonly consumed raw or blanched as side dishes or 'ulam' during meal times. Aside from shoots, other parts of the plant are also consumed in traditional medicines for the prevention and treatment of various diseases. As cancer is one of the leading cause of death in Malaysia, this study was aimed to determine the anti-proliferative effects of cashew shoots in various types of cancer cell lines. **Methods:** The shoots of cashew was obtained from Taman Botani, Universiti Putra Malaysia and extracted with 70 % ethanol. The selected cancer cell lines were breast cancer (MDA-MB-231) cells, liver cancer (HepG2) cells and colorectal cancer (HT-29) cells. The cells were treated with extracts of cashew shoots for cytotoxicity test using MTT assay. The extracts that demonstrated the IC50 value below 100 µg/ml were selected for further determination of apoptosis response using AO/PI dual fluorescent assay and cell cycle progression using flow cytometry. **Results:** The results showed that cashew shoot extract had IC50 of 81.1 µg/ml, 307.5 µg/ml and 272.6 µg/ml against MDA-MB-231, HepG2 and HT-29 cells, respectively. The results of AO/PI staining showed typical signs of apoptosis such as chromatin condensation, nuclear fragmentation and cell blebbing were markedly induced in treated- MDA-MB-231 cancer cells with cashew shoots extracts after 24, 48 and 72 hours in time-dependent manner. The results from cell cycle analysis showed significant increase in subG0 phase indicating apoptosis and significant decrease in G0/G1 phase in a dose-dependent manner. **Conclusion:** Cashew shoots extracts showed cytotoxicity towards selected cancer cells and have the potential to be studied further to understand underlying mechanism of the cashew extracts in cancer cell lines and possibility to be developed as nutraceutical or functional food products.

Keywords: Cytotoxicity, Apoptosis, Cell cycle, Breast cancer cells

Poster Presentation

DNA Methylation Status and Gene Expression of ErbB Family in Colorectal Cancer Cell Lines

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ABSTRACT

Introduction: Colorectal cancer (CRC) is the second most common malignancy in Malaysia. Recurrence of CRC cancer remains a major issue which affects nearly 50% of patients treated by conventional therapeutics. Despite many advanced therapies, many cases of recurrence and resistance have been reported. In recent years epigenetic changes including DNA methylation has been recognized to play a lead role in carcinogenesis. These changes have been hypothesized to be key players for diagnosis, prognosis and treatment of CRC. Aberrant DNA methylation of *ErbB* family has been implicated in the molecular pathogenesis of CRC. ErbB family, which consists of *EGFR (HER1), HER2, HER3* and *HER4*, plays a vital role in the regulation of cell proliferation, survival, and differentiation. Therefore, the objective of this study was to determine the gene expression and DNA methylation status of *EGFR, HER3* and *HER4* in colorectal cancer cell lines. **Methods:** CRC cell lines (HCT 116, HT-29, and Caco2) and normal colon cell line (CCD841 CoN) were obtained from ATCC and cultured in appropriate media supplemented with foetal bovine serum and 1% penicillin/streptomycin and under conditions described by ATCC. Total RNA was extracted from all cell lines using the RNeasy Plus Mini Kit and followed by reverse transcription to cDNA. The expression of *EGFR, HER3* and *HER4* were analysed using qPCR with *BETA-ACTIN* as reference gene. DNA was extracted from all cell lines using QIAamp DNA FFPE kit (Qiagen) followed by bisulfite conversion using Epitect Bisulfite Conversion Kit (Qiagen). The DNA methylation status of ErbB family were analysed using methylation specific PCR (MSP). Gel electrophoresis of the PCR and MSP products were carried out using 1% agarose gel. **Results:** *EGFR* and *HER3* were discovered to be unmethylated in HT-29, HCT 116 and Caco-2. Interestingly, *HER4* was methylated in HT-29 and HCT 116 but was partially methylated in Caco-2. For gene expression, *EGFR, HER3*, and *HER4* were upregulated in HCT 116, HT-29 and Caco-2 as compared to normal cell line. **Conclusion:** This study discovered that *EGFR, HER3* and *HER4* family were aberrantly expressed in colorectal cancer cell lines. DNA methylation may contribute to the regulation of these three genes. This preliminary study was beneficial for further studies in identifying ErbB family as potential CRC biomarkers and therapeutic targets.

Keywords: Colorectal cancer, DNA Methylation, Biomarkers

Poster Presentation

Engineering Recombinant Newcastle Disease Virus for Pro-Apoptotic Gene Delivery into Tumor Cells

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ABSTRACT

Introduction: Oncolytic viruses such as Newcastle disease virus (NDV) has been reported to be a suitable vector for targeted gene delivery to enhance oncolysis. Since NDV is an avian virus, it is generally eradicated by the human immune system through inflammatory responses, thus making it safe for humans. However, this interaction also reduces virus replication in cancer cells therefore compromising its ability to result in a more efficient oncolysis. Moreover, the emergence of NDV-apoptosis resistant tumors also limits its tumor cell tropism. **Methods:** In this study, the utilisation of NDV as a vector for pro-apoptotic, transgene delivery into tumor was explored. **Results:** Recombinant anti-genomic plasmid was successfully constructed by inserting the pro-apoptotic gene into the M and F intergenic region of the NDV anti-genome. The genetically modified NDV harboring the target transgene was successfully recovered by transfection of anti-genomic plasmid into BHK cell line and virus propagation in embryonated chicken eggs. The viral replication kinetics of the recovered virus was found to be similar to wild-type virus. Its oncolytic ability against EJ28 bladder cancer cells was also found to be significantly better compared to the wild-type virus based on MTT assay. Future work will examine expression of transgene by the engineered NDV infected cancer cells and analysed through Western Blot. The virus will also be subjected to *in vivo* antitumor study on nude mice challenged with EJ28 cells via intratumoral injection. Reduction in tumor sizes by engineered virus infection will be analysed and compared against those treated with wildtype NDV to evaluate overall therapeutic and gene delivery efficiency. **Conclusion**: The significance of this study was the generation of enhanced oncolytic viruses which may be more efficient against both primary and therapy resistant tumors through the extension of the tropism of NDV.

Keywords: Newcastle Disease Virus, NDV, Reverse Genetics, Apoptosis.

Poster Presentation

Recovery of a Novel Recombinant Newcastle Disease Virus from Strain AF2240-I with Reduced Virulence

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ABSTRACT

Introduction: Newcastle disease virus (NDV), an avian paramyxovirus, has long been studied for its antitumor effects through its oncolytic activity on several cancer cell lines. The virus can be categorized into three pathotypes: lentogenic, mesogenic, and velogenic depending on its effect on birds. Strain AF2240-I, a Malaysian strain, is a velogenic strain which has shown great oncolytic potential on several cancer cell lines; however, there is difficulty for it to enter clinical studies due to the potential harm that it may cause to the poultry industry. The virus is made up by six genes; but to date the key virulence factors have been reported to be the F, V, and HN proteins. **Methods:** In this study, the P gene of the NDV was mutated to create a strain with truncated V protein, and hence with reduced virulence. Site-directed mutagenesis using overlap extension PCR was performed to introduce a premature stop codon in the V protein. Sequencing was then done to confirm the mutation. The recombinant plasmid, along with helper plasmids were transfected into BHK cells stably expressing the phage T7 RNA polymerase to produce recombinant NDV. The virus pathogenicity will be tested using mean death time (MDT) and intracerebral pathogenicity index (ICPI). **Results:** The mutated fragment produced using overlapping PCR was of the correct size and was gel purified. The fragment and full length NDV plasmid digested with the same pair of restriction enzymes, purified and ligated produced a mutated NDV plasmid. The plasmid was then transformed into *Escherichia coli.* Positive clones were selected and plasmid was extracted followed by DNA sequencing. **Conclusion:** The recombinant NDV is expected to have a lower pathogenicity while retaining its strong anticancer properties and thus can be proceeded for further studies.

Keywords: Newcastle disease virus, oncolytic virus, virus recovery

Poster Presentation

Anti-proliferative Effect of Green Tea Epigallocatechin-3-gallate (EGCG) on Colorectal Cancer HT-29 Cell Lines: A Cytotoxicity Analysis

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ABSTRACT

Introduction: Traditional Chinese medicine has recommended drinking green tea for the prevention of disease. In recent years, many scientific and medical studies suggested that green tea possesses anti-proliferative, anti-mutagenic, antioxidant, antibacterial, antiviral and chemopreventive effects. One of the most abundant and bioactive compounds in green tea, epigallocatechin-3-gallate (EGCG) has demonstrated its role as the key player in various disease treatment and prevention including in colorectal cancer therapy. The ratio of mortality to incidence of colorectal cancer was reported to be 0.46 according to Malaysia's National Cancer Patient Registry Colorectal Cancer from the year 2008 till 2013. This study reports the anti-proliferative effect of green tea EGCG on a human adenocarcinoma colorectal cancer (HT29) cell line to find out the possible concentrations of EGCG required as reference for further use in molecular analysis, as part of colorectal cancer therapy. **Methods**: The MTT [3-(4,5dimethylthiazol-2-yl)2,5-diphenyltetrazolium bromide] assay was performed for assessing cell proliferation activity and cytotoxicity in HT-29 cells when treated with different EGCG concentrations ranging from 0 – 1000 μM at three different treatment periods; 24, 48 and 72 hours. The source of EGCG was from pure green tea purchased from Sigma (Product No. E4143). **Results:** The MTT results showed that effective EGCG concentrations to inhibit 50% of HT-29 cell proliferation (IC50) were 262.5 μM, 190.3 μM and 88.1 μM after a 24, 48 and 72 hours treatments, respectively, in dose- and time dependent manners. **Conclusion:** This study concludes that green tea EGCG does have an anti-proliferative effect on colorectal cancer cells, which may lead to suppression of colon carcinogenesis. The potential anti-proliferative effect of EGCG in colorectal cancer cells should be further examined to understand it's mechanism of actions as an anti-cancer agent.

Keywords: Tea, Epigallocatechin gallate, Colorectal cancer cells, Cell proliferation

Poster Presentation

Characterisation of Notch Signalling in Putative Bladder Cancer Stem Cells

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ABSTRACT

Introduction: Notch signalling is a canonical pathway which is involved in the regulation of stem-cell renewal and proliferation. This pathway has also been implicated in tumourigenesis, however, it often plays different roles in different cancers. Emerging data has shown that Notch receptor mutations are associated with bladder cancer but it is unclear whether Notch signalling also plays a role in regulating putative bladder cancer stem cells (CSCs). **Methods:** The objective of this study was to characterise Notch signalling in putative bladder CSCs population from bladder cancer cell lines. To achieve this objective, the putative bladder CSCs were selectively enriched in 3D culture condition using low-attachment plates. **Results:** Here we showed that the enriched spheroids expressed high levels of stem-cell associated genes implicating stemness in the cells. Expression of cell surface markers were evaluated and we showed that the expression levels of these markers in monolayer and spheroid cells were variable, suggesting, unsurprisingly, a diversity in the signatures of these cell lines. Analysis of Notch signalling components gene showed that expression level of certain NOTCH-related genes were significantly higher in the spheroid cells suggesting that these genes could be the candidate genes that can be further explored to study the putative bladder CSCs. The inhibition of gamma-secretase enzyme, a key component of the Notch signalling, using a gamma-secretase inhibitor could affect the proliferation of the bladder cancer spheroid. **Conclusion:** In summary, this study showed that Notch signalling could potentially maintain the proliferation and development of putative bladder CSCs. Inhibiting Notch signalling through the inhibition of gamma-secretase can be further explored as a potential therapeutic agent to target these cells.

Keywords: Cancer stem cells, Bladder cancer, Notch signalling, Gamma-secretase

Poster Presentation

Effects of Flower *Acmella uliginosa* (Swartz) Cass. on a Human Breast Cancer MCF-7 Cell Line and its Correlation with Metabolites Composition– GCMS based Metabolomics Approach

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ABSTRACT

Introduction: In-vitro cytotoxicity screening is a useful tool for the discovery of new potential anticancer agents from natural products. *Acmella uliginosa* (Swartz) Cassini; locally known as 'Pokok Getang' or 'Subang Nenek' has been used to relieve pain associated with toothaches. **Methods:** The present study investigated the correlation between untargeted metabolites and cytotoxicity effects of methanol crude of *A. uliginosa* flower on human breast cancer MCF-7 cells. All metabolites were determined by Gas Chromatography Mass Spectrometry (GCMS) analyses and the resulting chromatograms were exported to R version 2.13.0 (2011-04-13) software for peak selection. The relationships among the metabolites and cytotoxicity effects were evaluated using Orthogonal Projection to Latent Structure-Discriminant Analysis (OPLSDA) models in SIMCA13 software. **Results:** The GCMS data revealed the alkylamides were the major compounds in *A. uliginosa* flower. The inhibitory concentrations (IC50) of flower crude extract were 72.7µg/ml and 62.9µg/ml at 48 and 72 hours of treatment, respectively. The OPLS-DA model successfully discriminated the metabolites contributing to the cytotoxicity effects which both alkylamides; N-isobutyl-2(E),6(Z),8(E)-decatrienamide and N-isobutyl-2E,4Z,8Z,10E-dodecatetraenamide were identified attributing significantly to cytotoxicity effects on human breast cancer MCF-7 cell line. Alkylamides are known to have inhibition activities towards cyclooxygenase-1 and -2 (COX-1 and COX-2) and 5lipooxygenase that contribute to cancer and metastasis development. **Conclusion:** The proposed method of using multivariate data analysis to evaluate GCMS chromatograms in combination with cytotoxicity effects was successfully applied to identify active biomarkers.

Keywords: *Acmella uliginosa*, GCMS, Orthogonal Projection to Latent Structure Discriminant Analysis (OPLS-DA), Metabolomics, Cytotoxicity

Poster Presentation

Effects and Mechanisms of Citral in Targeting Breast Cancer Aldehyde Dehydrogenase (ALDH)-Positive Spheroids

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ABSTRACT

Introduction: Breast cancer remains a leading cause of death in women worldwide. Although breast cancer therapies have greatly advanced in recent years, many patients still develop tumour recurrence and metastasis, and eventually succumb to the disease due to chemoresistance. Citral has been reported to show cytotoxic effect on various cancer cell lines. However, the potential of citral to specifically target the drug-resistant breast cancer cells has not yet been tested, which was the focus of our current study. **Methods:** The cytotoxic activity of citral was first tested *in vitro* on MDA-MB-231 and MCF-7 breast carcinoma cells by MTT assay. Subsequently, spheroids of MDA-MB-231 and MCF-7 cells were developed and treated with citral at different concentrations. Doxorubicin, cisplatin and tamoxifen were used as positive controls to evaluate the drug resistance phenotype of MDA-MB-231 and MCF-7 spheroids. In addition, apoptosis study was performed using Annexin V/7AAD on flow cytometry. Aldefluor assay was also carried out to examine whether citral could inhibit the ALDH-positive population, while the potential mechanism of the effect of citral was carried out using quantitative reverse transcriptase-PCR followed by western blotting analysis. **Results**: Citral inhibited the growth of the MDA-MB-231 spheroids at a lower IC50 value compared to the monolayer culture of MDA-MB-231 cells. To confirm the inhibition of spheroid self-renewal capacity, the primary spheroids were then cultured to additional passages in the absence of citral. There was a significant reduction in the number of formed secondary spheroids, suggesting the reduction of self-renewal capacity of these ALDH+ drug resistant spheroids. Moreover, the annexin V/7AAD results demonstrated that citral induced both early and late apoptotic changes in a dose-dependent manner compared to the vehicle control. Furthermore, citral-treated spheroids showed lower cell renewal capacity compared to the vehicle control spheroids in the mammosphere formation assay. Gene expression studies using quantitative reverse transcriptase-PCR and Western blotting assays showed that citral targeted the self-renewal capacity of spheroids via inhibition of the Wnt/β-catenin pathway. **Conclusion:** The results suggested that citral could be a potential new agent to eliminate drug-resistant breast cancer cells in a spheroid model via inducing apoptosis and inhibiting Wnt-mediated cell renewal pathway.

Keywords: Citral, Wnt, Spheroids, ALDH1

Poster Presentation

Impact of a Health Education Intervention Program on Breast Self-Examination among Female Undergraduate Students in Klang Valley, Malaysia

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ABSTRACT

Introduction: Breast cancer is the most common cancer and the second principal cause of cancer deaths in women worldwide as well as in Malaysia. The present study aimed to assess the impact of a health educational intervention to improve knowledge and practice breast self-examination (BSE) among female undergraduate students in Klang Valley, Malaysia. **Methods:** Randomized Community Trial study was carried out in three phases; pre intervention phase, intervention phase, and post intervention phase. A total number of 396 female undergraduate students from two public universities in Klang Valley, Malaysia participated in this study. The students were randomly divided into intervention (n = 198) and control (n=198) groups. Interventional health education in the form of a lecture, which supported by an educational model, presentations were administered. Data were collected within January 2011- March 2012. **Results:** The mean age of participation was 21.7 years, majority of them were Malay 380 (96%), Muslim 376 (94.95) and single 381 (96.2). The results showed that there was a significant improvement in knowledge regarding all aspects of breast cancer and breast self-examination of the intervention group from pre- to post-tests. After intervention, about 33.3% practiced breast self-examination (BSE) in post-test compared to 22.2% who practiced it in pre-test. Also, there were statistically significant differences between those who practice and did not practice BSE in term of knowledge score of BSE (p-value <0.05). There was no association between breast self-examination and (age, race, family history of breast cancer) (p value <0.05). **Conclusion:** The knowledge and practices of women toward breast self-examination for early detection were observed to be inadequate in respondents but there was a significant improvement after the intervention.

Keywords: Breast self-examination, Breast cancer, Health education, Knowledge, Malaysia

Poster Presentation

Evaluation of Selected Reference Genes in Acute Myeloid Leukaemia

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ABSTRACT

Introduction: Quantitative analysis of gene expression is an essential tool in the study of biological systems and elucidation of diseases. Reliable and accurate results are dependent on selecting the right reference gene. Criteria for this endogeneous control include stable, constitutive expression in all nucleated cells among different analysed samples to compensate for uneven cell numbers, RNA quality or variations in reverse transcription efficiencies, of individual samples. Previous selections were based on assumption that proteins essential for cell function such as cytoskeleton, major histocompatibility complex, enzymes of metabolic pathways provide stable expressions. However, recent reports suggest expression of these genes varied considerably among tissue samples. Thus, the objective was to compare selected reference genes for gene expression analysis in acute myeloid leukaemia (AML). **Methods:** A potential reference gene (*SRP14*) identified from an earlier study based on small coefficient of variation (CV) and a maximum fold change <2 (MFC, the ratio of the maximum and minimum values observed within the dataset) and another commonly used reference gene, beta-microglobulin (*B2M*) were selected. Quantitative polymerase chain reaction (Q-PCR) method was used to determine expression of 13 (*ATP5B, CALM2, CSTB, H2AFZ, EIF3M, TMSB4X, PBX3, SON, DDB2, PDCD61P, PGK1, SELL* and *SF3B1*) AML-associated genes in 16 AML samples and 16 healthy controls (HC). **Results**: CV and MFC in leukaemia samples and healthy controls were higher in *B2M* (CV=14.6, MFC=1.7 and CV=19.4, MFC=1.7, respectively) compared to *SRP14* (CV=10.4, MFC=1.4 and CV=4.8, MFC=1.2, respectively). Mann-Whitney statistical test analysing with *SRP14* as reference gene, 9 genes (*ATP5B, CALM2, CSTB, PBX3, SON, DDB2, PGK1, SELL* and *SF3B1)* were significantly different ($p<0.05$) between AML and HC. With *B2M*, only three genes (*CALM2, SON* and *DDB2*) were significantly different ($p<0.05$). **Conclusion:** *SRP14* showed more stable expression than *B2M* and may serve better as a reference gene in AML. Disease specific selection of reference gene may be a necessary consideration in gene expression analysis.

Keywords: Reference gene, AML, SRP14, B2M

Poster Presentation

EGFR and HER3 Expression in Primary Colorectal Adenocarcinoma

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ABSTRACT

Introduction: Colorectal cancer (CRC) is the second most reported cancer in Malaysia. Although there are advancements in cancer therapy research, CRC is still facing challenges with 50% relapses risk and treatment resistance issues. Responding to these problems, many studies have been conducted to improve and search for new potential biomarkers. Efficient biomarkers are in need for prognostic and more competent therapeutic regimens. Tyrosine kinase receptors (TKR) including epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor-3 (HER3) are classified as cell surface receptors and were related to prognosis and therapeutic assessment in many of CRC cases. Analysing two related biomarkers brings more information with the potential to serve as dual targeted antibodies. This study aims to evaluate EGFR, HER3 and EGFR/HER3 immunohistochemical expressions in CRC, with the hope of determining its possible relationship with demographic and clinicopathologic parameters. **Methods**: 94 samples were retrieved from Department of Pathology, Hospital Serdang archive between the year 2008 and 2015. Tissue sections were made from formalin fixed paraffin embedded (FFPE) samples of primary colorectal adenocarcinoma. EGFR and HER3 protein expressions were tested using immunohistochemistry (IHC). IHC staining was scored with semi-quantitative scoring system. Association of EGFR, HER3 and EGFR/HER3 expressions with demographic and clinicopathologic parameters were evaluated using chi-square test. **Results:** Immunopositivity were found in 42.6% of CRC samples in both EGFR and HER3 staining. EGFR cytoplasmic and luminal side of cell membrane expression was associated with non-Malay (p=0.038) and non-diabetic (p=0.044) samples. The cytoplasmic expression of HER3 was found to be more in females (p=0.027) and lymph node metastasis (p=0.049). EGFR expression was associated with HER3 expression (p=0.001) and EGFR/HER3 co-expression was related to moderate tumour grading (p=0.030). **Conclusion**: EGFR and HER3 were found to be overexpressed in CRC samples. Their expressions may indicate potential prognostic factors with more advanced tumour conditions. Co-expression of EGFR and HER3 pairs may play a crucial role for adjuvant therapy as dual targeted antibodies.

Keywords: Colorectal cancer, EGFR expression, HER3 expression, Immunohistochemistry, Biomarker

Poster Presentation

Cytotoxic Effect of Rambutan Skin Extract Containing Triterpenoid Saponin on a Leukaemia Cell Line

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ABSTRACT

Introduction: Triterpenoid saponin is a compound found in various plants and has anticancer properties in various human cancer cell lines. Earlier screening test on rambutan skin extract indicated the presence of triterpenoid saponin. Further studies on its anticancer property may provide further evidence of its potential as a recyclable source of waste product and development as an adjunct to the current therapeutic regimens available for human cancers. This study investigated the triterpenoid saponin content and anticancer effect of rambutan skin extract on a human leukaemia cell line. **Methods:** A T cell leukaemia cell line, Jurkat was expanded in RPMI culture media supplemented with 10% fetal bovine serum, and antibiotics. Rambutan skin was dried and then macerated overnight in 96% ethanol. The solution was filtered and the crude extract used for further testing. Screening for saponin was performed using foam and haemolytic test. Presence of triterpenoid was determined with the Salkowski test. Cytotoxic effect of rambutan skin extract was determined using the MTS assay with a series of 2X extract dilution ranging from 1/64 to 1/1024. Cells were cultured for 48 hours. **Results:** Foam, haemolytic and Salkowski tests demonstrated the presence of triterpenoid saponin in ethanolic rambutan extract. Jurkat cells treated with extract exhibited cell death/inhibition as observed under the microscope. Control wells treated with diluted 96% ethanol showed cell inhibition only at high concentrations. The IC50 dilution from the MTS assay was determined to be 1/200. **Conclusion:** Rambutan skin extracts in ethanol contain triterpenoid saponin and exhibited cytotoxic/inhibitory effect on Jurkat cell line.

Keywords: Triterpenoid saponin, Jurkat, Rambutan skin extract, Ethanol, IC50

Poster Presentation

Gene Profiling of Anti-Tumour Activity of Umbilical Cord Mesenchymal Stem Cells on Lymphoid Origin Tumour Cell Proliferation

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ABSTRACT

Introduction: Cancer represents one of the major health issues all over the world. Currently, conventional therapies have not yielded satisfactory outcomes; hence, there is a need for an effective cancer therapy. Past research studies have demonstrated that umbilical cord-derived mesenchymal stem cells (UC-MSCs) inhibit the growth of various tumour cells. However, the molecular mechanisms that execute this MSCs-mediated anti-tumour activity are still elusive. Therefore, analysis of molecular mechanism and pathway may lead to improved understanding of UC-MSCs' anti-proliferative activity as a novel therapeutic tool. **Methods:** The isolated cells from human umbilical cord Wharton's Jelly were characterised by immunophenotyping and mesodermal differentiation capacity and subsequently co-cultured with lymphoid origin tumour cells. The effect of UC-MSCs on tumour cell proliferation was assessed by 3H-TdR uptake assay, and the mode of inhibition was evaluated by transwell, apoptosis and cell cycle assays. Finally, the global gene expression was gauged with microarray assay to determine the molecular mechanism and signalling pathways involved in the antiproliferative effect of UC-MSCs. The microarray results were further validated by RT-qPCR of selected genes. **Results**: UC-MSCs inhibited the growth of lymphoid origin tumour cell line through a cell-to-cell contact mode with no sign of apoptosis induction and via arresting the target cells in G0/G1 and S phase of cell cycle. Subsequently, BV173 cell line, a B cell leukaemia lineage was subjected to the microarray experiment. The microarray results showed 3019 differentially expressed genes (DEGs) in BV173 with FC>2 and p-value<0.05. The *in silico* analysis illustrated the DEGs which functionally were associated with cell adhesion, cell migration, cell cycle control, cell growth and proliferation clusters. Moreover, several DEGs were implicated in 11 cancer-related diverse signalling pathways such as focal adhesion, PI3K/AKT, MAPK, TGF-beta signalling pathway and more. The most alteration in gene expression in signalling above pathways is related to oncogenes or tumour suppressor genes. **Conclusion:** The present study showed that UC-MSCs suppressed tumour cell proliferation via perturbation in the cell cycle of the tumour cell. The reported changes in biological activities of tumour cells were driven by the changes in expression of genes either involved in the cell adhesion, cell proliferation (oncogenes and tumour suppressor genes), cell cycle and ECM signalling pathways and/or twisted in the inflammatory microenvironment.

Keywords: Umbilical cord, Mesenchymal stem cell, lymphoid origin cancer cell, Gene profiling, cell cycle

Poster Presentation

Emulsification-Solvent Evaporation Method for Development of Nanoparticles from Preformed Polymers for Cancer Drug Delivery

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ABSTRACT

Introduction: Cancer is still one of the most destructive disease group for human body in the world due to the complexity and progressive nature of the cancer diseases. To date, various types of anti-cancer drugs have been developed specifically to treat several types of cancer. Nevertheless, the drugs have poor water solubility, high toxicity to neighbor cells, short blood circulation time and comes with low therapeutic efficacy which makes this disease still need novel and effective diagnosis and treatment strategies. The application of nanoencapsulation is very much suggested to improve the solubility of the drugs and other factors mentioned. Nanoparticles provides better advantage than conventional drugs since it can deliver hydrophilic and hydrophobic drug molecules to the targeted area. Emulsification-solvent evaporation, solvent emulsification-diffusion, salting-out, nanoprecipitation, supercritical fluid technology and dialysis are commonly used methods to produce nanocapsule. Method selection can be made based on factors like particle size, particle size distribution and area of application. Emulsification-solvent evaporation method was chosen for this study since it is the most widely used methods in nanoparticles preparation from the preformed polymer. **Methods:** Prefromed polymer dissolved in a volatile solution (DCM, $CHCL_3$ or $C_4H_8O_2$) and turned into an aqueous phase during emulsification process. The dissolved drug particles in the solution were dispersed in the polymer matrix network with the aid of dispersing agent and high-energy homogenisation. In the second step, the solvent used was evaporated from the solution via temperature increasing under pressure or through continuous stirring to obtain nanospheres. During the addition of the solvent into the emulsifier, ultrasonication was needed to stabilise the small organic droplets and obtain a homogeneous oil-in-water emulsion. Centrifugation was used to collect the nanoparticles. The nanoparticles obtained were washed with distilled water to remove the residue of stabilizer or any unencapsulated drugs and lyophilized for storage purposes. **Results:** It was found that by the increase in homogenization rate and surfactant concentration, size of the nanoparticles was decreased, while the size was increased by the increase in polymer/solvent ratio. **Conclusion:** The emulsification-solvent evaporation method is the most widely used methods in nanoparticles preparation from the preformed polymer. Single-emulsions preparation, the oil-in-water emulsion and double-emulsions preparation, the water-in-oil-in-water are available. The oil-water emulsions become an attention due to the usage of water as the nonsolvent. This will cause no recycling process, simplifies and improves process economics, simplifies the washing step and reducing agglomeration.

Keywords: Nanoencapsulation, Preformed polymer, Anti-cancer drug, Emulsification-solvent evaporation, Target delivery

Poster Presentation

Phytochemical Screening and Cytotoxicity of Crude Extracts from the Seed of *M. oleifera* against Breast, Liver and Prostate Cancer Cell lines

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ABSTRACT

Introduction: This study was carried out to investigate the phytochemicals and cytotoxicity of *M. oleifera* seed extracts on Human breast adenocarcinoma cell line (MCF-7), Human hepatocellular carcinoma cell line (Hep G2) and two Human prostate carcinoma cell lines (PC-3 and DU 145). **Methods**: The seeds were soaked overnight to defat and subsequently extracted in water, hexane, chloroform, acetone, methanol and ethanol followed by phytochemical screening and cytotoxicity in various cancer cells. **Results:** Crude water extract yielded the highest amount of crude (21.78 %), followed by methanol (11.79 %), hexane (5.33 %), ethanol (1.28 %), chloroform (0.71 %) and acetone (0.51 %) (w/w). The phytochemicals screening showed the presence of saponin, coumarin, alkaloid, quinone and fat in several crude extracts. As for cytotoxicity assay, the crude extracts were tested on breast, liver and two prostate cancer cell lines. After 72 hour of treatment with the crude extracts, MTT assay were done to determine the IC_{50} value. Crude water extract showed the lowest IC_{50} value on MCF-7 (18.60 µg/mL) and DU 145 (18.24 µg/mL) and PC-3 (4.12 µg/mL). Crude chloroform and acetone extracts also showed low IC_{50} value on DU 145 cell line with 19.55 µg/mL and 19.33 µg/mL, respectively. In addition, chloroform extract showed the lowest IC_{50} value on Hep G2 (16.61 µg/mL). **Conclusion:** In this study, crude water, chloroform and acetone extracts of *M. oleifera* seed were found to be active against breast, liver and prostate cancer cell lines. It can be concluded that the extracts from *M. oleifera* seeds have a great potential for breast, liver and prostate cancer treatment.

Keywords: Phytochemicals, Cytotoxicity, *M. oleifera*, Crude extracts

Poster Presentation

Haematological Effect and Serum Cardiac Biomarker Assessment of Cockle Shell Derived Calcium Carbonate Nanoparticle-Doxorubicin on Experimental Healthy Dogs

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ABSTRACT

Introduction: Cockle shell-derived calcium carbonate nanoparticle (CS-CaCO3NP) is a biodegradable carrier with sustained release potential in drug delivery. Doxorubicin is a known potent anticancer associated with off-target effects on healthy cells causing myelosuppression and cardiac dysfunctions. Although many organic nanomaterials are employed for the delivery of doxorubicin. Thus, this study was aimed at evaluating the hematopoietic effects and monitoring of the serum cardiac biomarker upon administration CS-CaCO3NP-DOX in healthy dogs. **Methods:** A total of 15 healthy dogs with an average body weight of 15-25 kg were randomized into 5 groups (n=3). Dogs were subjected to slow intravenous infusion up to 5 doses every 3 weeks interval with (i) normal saline (control), (ii) doxorubicin 30 mg/m2, (iii) CS-CaCO3NP-DOX (experimental groups) of different concentration (50 mg/m2, 30 mg/m2, & 20 mg/m2). Blood was collected for haematological, biochemical assays and cardiac injury biomarkers assessments. **Results:** A cumulative dose of 150 mg/m2 of doxorubicin over 15 weeks of duration revealed haematological alterations and serum cardiac biomarkers elevations as compared to experimental groups with no significant hematopoietic alteration and serum cardiac biomarkers in the dog's given equivalent doses of CS-CaCO3NP-DOX over time. Low levels of RBC, WBC, haemoglobin and platelets were observed with free DOX (30 mg/m2) as compared to it equivalent dose of CS-CaCO3NP-DOX. Cumulative dose below CS-CaCO3NPDOX 150 mg/m2 did not show any significant elevation in serum biochemical and cardiac injury biomarkers as compared to the dogs in the control group and dogs given an equivalent dose of the free doxorubicin. **Conclusion:** The study confirmed the safety of the repeated dose administration of CS-CaCO3NP DOX (30 mg/m2) to dogs with no haematological and cardiotoxic effects. This finding offers great optimism in reducing side effects of DOX in dogs with cancer that may benefit from long term therapeutic regimes of doxorubicin.

Keywords: Haematological, Cardiac biomarkers, CS-CaCO3 nanoparticle, Doxorubicin, Hematopoietic cells.

Poster Presentation

DNA Methylation of Survivin and Expression in Colorectal Cancer Cell Lines

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ABSTRACT

Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide and is the second leading cancer in Malaysia. Beside genetic alterations, cancer initiation and cancer progression are also influenced by epigenetic modifications, especially DNA methylation. Cancer cells show aberrant DNA methylation at the promoter region of many genes. Survivin is a novel antiapoptosis gene that is prominently expressed in CRC. Its over-expression is believed to be influenced by DNA hypermethylation. Despite that methylation pattern is heritable, it is reversible, making it a potential therapeutic target in CRC through demethylation approach. Therefore, the objective of this study was to determine the association between DNA methylation status and mRNA level of Survivin in CRC cell lines. **Methods:** CRC cell lines (HCT116 and HT29) and a normal colon cell line (CCD841) were obtained from ATCC. Cells were cultured in appropriate media supplemented with foetal bovine serum and 1% penicillin/streptomycin as described by ATCC. Total RNA was extracted from all cell lines followed by reverse transcription to cDNA by using RNeasy Plus Mini Kit and QuantiTect Reverse Transcription Kit, respectively. Expression of Survivin was analysed using qPCR and Beta-actin was used as the reference gene. Promoter methylation was identified using methylation specific PCR (MSP). DNA was extracted from the cell lines by using QIAamp DNA FFPE kit (Qiagen) and then was proceeded with bisulfite conversion by using Epitect Bisulfite Conversion Kit. The PCR and MSP products were electrophoresed on 1% agarose gel. **Results:** Survivin expressions were upregulated and promoter were hypomethylated in both cancer cell lines as well as the normal cell line. **Conclusion:** This study identified that Survivin was prominently expressed in colon adenocarcinoma cell lines. However, methylation analysis was not able to confirm involvement at the site examined. This preliminary study supports the potential of Survivin as a CRC biomarker and remain a potential therapeutic target but may require examination of other promoter sites involved in cancer induced methylation modification.

Keywords: Colorectal cancer, Survivin, DNA methylation

Poster Presentation

Knowledge of Breast Cancer and Practices Concerning Clinical Breast Examination among Yemeni Female School Teachers in Malaysia

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ABSTRACT

Introduction: Breast cancer is the most prevalent cancer and considered the second leading cause of cancer deaths in females worldwide, including Yemeni women. The aim of this study is to assess breast cancer knowledge and clinical breast examination (CBE) practice among Yemeni female school teachers in Malaysia. **Methods:** A cross-sectional study was implemented among 163 Yemeni female school teachers in Malaysia between April 2017- May 2017. A simple random sampling method was adapted and a validated self-administered questionnaire form was used to collect the data. **Results:** The mean age of respondents was 32.8 ±7.23 years, 128(78%) of them were married, 26 (15.9%) had a family history of breast cancer and 34 (20.9%) of them have previously participated in a breast cancer education program. It was observed that majority of respondents 131(79.9%) heard/read about breast cancer screening, but only 34(20.9%) reported that they have practiced clinical breast examination and 104(63.8%) had the intention to practice CBE in the future. On the other hand, majority of respondents 121(74.2%) and 111(68.1%) had a low level of knowledge about breast cancer and CBE practice, respectively. Univariate analysis revealed that hear/read about breast cancer screening, participated in breast cancer education programs, CBE practice were significantly associated with knowledge of breast cancer. Also, participated in breast cancer education programs was significantly associated with CBE practice ($p<0.05$). **Conclusion:** Results of this study revealed that Yemeni female school teachers had poor knowledge of breast cancer and rare practice of clinical breast examination. It is recommended that health education programs should be developed to enhance knowledge regarding breast cancer and to improve CBE practice among this group.

Keywords: Knowledge of breast cancer, Clinical breast examination, Yemeni teachers, Malaysia.

Poster Presentation

Influence of Process Parameters in Particle Size and Morphology on Encapsulated Tamoxifen using Supercritical Anti-solvent (SAS) Process

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ABSTRACT

Introduction: Tamoxifen is an anti-cancer drug which has been extensively used in breast cancer treatment. While Tamoxifen has shown excellent recovery rate, patients who has been consuming Tamoxifen for a long period of time will experience side effects as mild or hot flushes to severe effect such as endometrial cancer. To reduce the side effects, Tamoxifen can be encapsulated in a biodegradable polymer. Supercritical anti-solvent process can be used to replace conventional processes in encapsulating drugs due to its advantages such as environmental friendly, elimination of usage of toxic solvent and a single step of encapsulation process. However, effect of encapsulated particle size and morphology of particles on variation of process parameters of SAS process has to be determined. **Methods**: A known amount of Tamoxifen and Poly-L-Lactic Acid were dissolved in Dichloromethane. The solution was fed to a precipitation vessel which has been charged with supercritical carbon dioxide. Operating parameters such as pressure of supercritical carbon dioxide, concentration of polymer, solution flow rate and temperature were varied. Final encapsulated particles were analysed using SEM analysis to determine its particle size and morphology. **Results**: Precipitation of encapsulated product occurred due to high supersaturation condition in vessel. Pressure ranging from 70 bar to 150 bar was used as set point in this study. Results showed that at below supercritical pressure, no products were formed due to the supercritical fluid condition were not met, thus precipitation of product does not occur. As pressure increases, density of supercritical fluid increased thus increasing mass transfer and producing smaller particle size. Moderate amount of polymer was required to encapsulate Tamoxifen, as increasing amount of polymer will promote agglomeration. Low solution feed flow rate was favourable due to increased residence time of solution in the nozzle which led to higher mass transfer. Small particle size with significantly reduced agglomeration were synthesized at temperature that was slightly above critical temperature. As temperature is higher, it will approach glass temperature of polymer thus will cause final product to agglomerate and increased in size. **Conclusion**: Tamoxifen was successfully encapsulated within PLLA via SAS process. The study showed that to have small and uniform particle size with non-agglomerated product, SAS has to be operated at high pressure and low temperature. Low flow rate of solvent has been chosen as the best flow rate. Amount of polymer has to be carefully selected as low amount of polymer will be unable to fully encapsulate Tamoxifen and high amount of polymer will promote agglomeration.

Keywords: Tamoxifen, Drug Encapsulation, Supercritical Fluid Supercritical Anti Solvent Process Biodegradable Polymer

Poster Presentation

Predicting Breast Cancer by Image Enhancement with RGB Coloring Technique on Mammogram

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ABSTRACT

Introduction: Breast cancer is the leading cancer in the world. Early detection in breast cancer increases the chances for successful treatment for the patient. Currently, Mammography is the gold standard for early screening for breast cancer because of its sensitivity. However, the accurate classification of breast abnormalities remains a medical challenge. The major problem is that mammogram is analyzed based on its original x-ray colors; black and white. These two colors lead computer-aided diagnosis (CAD) to predict with little information and subsequently affect accuracy. **Methods**: This paper presents a CAD for automatic classification of breast cancer using coloring technique for image enhancement. As for feature extraction, the features of colored mammogram are based on the relative brightness of red, green and blue channels on a mammogram. **Results**: Six RGB channels were extracted from colored mammogram images; using six-dimensional features vector of mammogram data for training and testing the classifiers. Artificial neural network and support vector machine were used for classification and their results were compared. **Conclusion**: The system predicts normal and malignant breast tissues.

Keywords: Image processing, Image enhancement, Computer-aided diagnosis, Breast cancer, Mammogram

Poster Presentation

Association of Tumour Necrosis Factor-Alpha with Survival of Nasopharyngeal Carcinoma in Malaysia

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ABSTRACT

Introduction: Tumour necrosis factor-alpha (TNFA) is an extraordinarily pleiotropic cytokine with an important role in inflammation, immune homeostasis and host defence. It can induce such diverse effects as necrosis, apoptosis, angiogenesis, differentiation, immune cell activation and cell invasion and migration which have great relevance in tumour immune surveillance, and also play crucial roles in tumour development and tumour progression. **Methods**: To further investigate the role of TNFA in nasopharyngeal carcinoma (NPC), an inflammation-related cancer, TNFA concentration was measured in serum samples from 300 histologically confirmed cases of NPC and matched 300 cancer free controls. Serum TNFA concentration was measured using Milipore's Milliplex MAP Human Adipocyte Magnetic Bead panel and Luminex 200TM analyzer. The survival probability of patients with NPC was estimated using the Kaplan Meier analysis. The association between serum TNFA and survival of NPC was determined by a multivariable Cox proportional hazard model. **Results**: Median TNFA values among cases was slightly lower compared to controls (0.002 ng/mL vs. 0.003 ng/mL) but was not significant (p = 0.147). Most of the cases were in the third quartile of TNFA (36.3%) while most of the controls were in the lowest quartile of TNFA (33.3%). The survival rate was highest at second quartile of serum TNFA concentration (73.7%, N =56) (χ^2 = 9.59, p = 0.022). In the adjusted survival analysis, the highest quartile (Q4) of TNFA significantly increased the mortality among NPC cases more than three-fold (AHR = 3.59, 95% CI = 1.32, 9.79) compared to the lowest quartile of TNFA (Q4). **Conclusion**: The findings suggest that serum TNF level could be an indicator for cancer progression, treatment response and prognosis. TNFA might promote local spread and metastasis of NPC via induction of inhibitor of apoptosis proteins, which further enhances the progression and metastasis of NPC as well as reduces the survival of NPC cases.

Keywords: Tumor necrosis factor-alpha, Nasopharyngeal carcinoma, Case-control, Survival, Malaysia