UPM
UNIVERSITI PUTRA MALAYSIA
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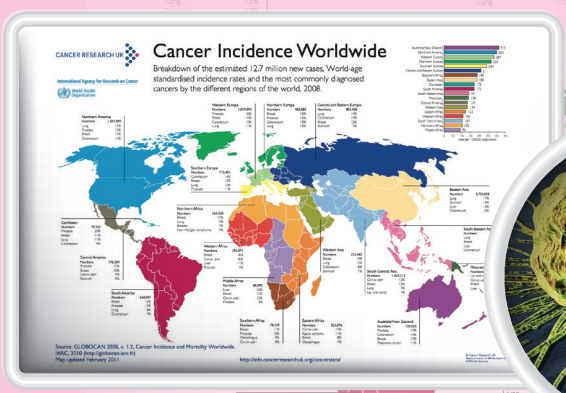
KESEDARAN
KANSER
2014

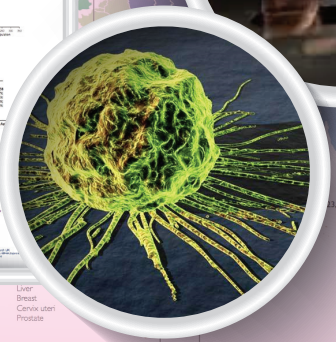
ABSTRACTS OF SCIENTIFIC CANCER RESEARCH POSTERS

in conjunction with

CANCER AWARENESS CARNIVAL 2014

Date : 10th May 2014
Venue : Faculty of Medicine and Health Sciences, Universiti Putra Malaysia





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CATEGORIES OF POSTER COMPETITION

1) Clinical / Nutraceutical / Pharmaceutical

2) Molecular Biology / Genetics

3) Social Sciences / Computer Applications / Others

SCIENTIFIC CANCER RESEARCH POSTER COMPETITION IN CONJUCTION WITH

CANCER AWARENESS CARNIVAL UPM 2014 PROGRAMME

	FIRST DAY: 8th MAY 2014 (THURSDAY)
8.30 am –3.00 pm	Preparation of poster board by secretariat
3.00 – 5.00 pm	Putting up of posters

	SECOND DAY: 9th MAY 2014 (FRIDAY)
8.00 am –9.00 am	Registration of participants Putting up of posters
9.00 am – 11.00 am	Judging Session
11.00 am – 12.00pm	Presentation of Certificate of Attendance

	THIRD DAY: 10th MAY 2014 (SATURDAY)
8.00 am –5.00 pm	Cancer Awareness Carnival 2014 & Poster Viewing
8.00 pm – 11.00 pm	Prize Giving Ceremony during the Charity Dinner

LIST OF TITLES

1) ISOLATION, PURIFICATION AND EVALUATION OF ANTICANCER PRINCIPLE FROM ZINGIBER ZERUMBET
2) CARBON NANOMATERIALS AS DRUG TRANSPORTER FOR CANCER THERAPY
3) *IN* VITRO ANTI-CANCER EFFECT OF LAYERED DOUBLE HYDROXIDE-CHLOROGENIC ACID NANOPARTICLES AS DRUG DELIVERY SYSTEM
4) PROTOCATECHUIC ACID-ZINC/ALUMINIUM LAYERED DOUBLE HYDROXIDE NANOCOMPOSITE AS AN ANTICANCER NANODELIVERY SYSTEM
5) CYTOTOXIC PROFILES OF A NANODRUG DELIVERY BASED ON 6-MERCAPTOPURINE-COATED MAGNETITE-PEG NANOPARTICLES TOWARDS LEUKEMIA (WEHI-3B) CELL LINES
6) *IN* VIVO ASSESSMENT OF NANOSTRUCTURED LIPID CARRIER FOR ORAL DELIVERY OF ZERUMBONE IN LEUKEMIC MICE MODEL
7) ANALYSIS OF PERIPHERAL BLOOD OF OVARIAN CANCER PATIENTS INDICATES HIGHER SUB-POPULATIONS OF NATURAL KILLER AND B CELLS COMPARED TO HEALTHY VOLUNTEERS
8) 'A FLY IN THE OINTMENT'
9) ANTI CANCER ACTIVITY OF MANGIFERIN FROM METHANOL EXTRACT OF FRUIT OF MAHKOTA DEWA (PHALERIA MACROCARPA (SCHEFF.) BOERL.)
10) CYTOTOXICTY OF ZERUMBONE AGAINST LIVER CANCER CELL LINES (HepG2) VIA APOPTOSIS ACTIVITY
11) TOXICITY EFFECT ON DIFFERENT TYPES OF TIGER MILK MUSHROOM EXTRACTS AGAINST HUMAN NORMAL LUNG CELL (MRC5) AND LUNG CANCER CELL (A549)
12) CYTOTOXIC EFFECTS OF BIO-SYNTHESIZED ZINC OXIDE NANOPARTICLES ON MURINE CELL LINES
13) EFFECTS OF GOLD NANOPARTICLES SYNTHESIZED USING WATER EXTRACT OF BROWN SEAWEED; SARGASSUM GLAUCESCENS
14) LINKAGE ANALYSIS BETWEEN PROSTATE CANCER OCCURRENCE AND Y-CHROMOSOMAL DYS LOCI IN MALAYSIAN MALE SUBJECTS
15) MIR-137-MEDIATED LOSS OF KDM5B EXPRESSION LEADS TO SUPPRESSION OF THE MALIGNANT PHENOTYPE OF BLADDER CANCER CELLS
16) BACTERIA AS POTENTIAL TUMOUR FIGHTER

17) CANINE MAMMARY GLAND TUMOURS DIAGNOSED AT VETERINARY HISTOPATHOLOGY LABORATORY, FACULTY OF VETERINARY MEDICINE, UNIVERSITI PUTRA MALAYSIA 2006 – 2012
18) OVEREXPRESSION OF CTAG1B IS A POTENTIAL BIOMARKER IN BLADDER CANCER
19) FIBROBLAST GROWTH FACTOR RECEPTORS: THEIR EXPRESSION AND CLINICOPATHOLOGICAL RELEVANCE IN CANINE MAMMARY GLAND TUMOURS
20) THE CYTOTOXCITY ACTIVITY OF *IN* VITRO ISOLATED AND EXPANDED CYTOTOXIC T-LYMPHOCYTES AND NATURAL KILLER CELLS IN BLADDER CANCER
21) THE DESIGN OF RESTORATIVE OUTDOOR ENVIRONMENTS FOR CANCER PATIENTS
22) O-CARECLOUD: OVARIAN CANCER PATIENT MANAGEMENT SYSTEM ON CLOUD
23) RANDOM WALKERS BASED BREAST THERMOGRAPHY IMAGE SEGMENTATION
24) COMPUTER AIDED DETECTION/DIAGNISIS FOR BREAST CANCER DETECTION IN COMPUTED TOMOGRAPHY LASER MAMMOGRAPHY (CTLM)
25) AN INTEGRATIVE CANCER CLASSIFICATION BASED ON GENE EXPRESSION DATA

ISOLATION, PURIFICATION AND EVALUATION OF ANTICANCER PRINCIPLE FROM *ZINGIBER ZERUMBET*

Heshu, S.R.[1,2,3], Hemn, H.O.[1,3*], Abdullah, R.[1,2], Chartrand, S.M.[4], Zeenathul, N.A.[1,2], Zahra, A.[5], Mahnaz, H.[2], Nozlena, A.S.[2]

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The Zingiberaceae family is found in tropical and subtropical areas, with approximately 161 species from 18 genera of this family found in Peninsular Malaysia. *Zingiber zerumbet* (L.) Smith tree belonging to this family is an edible ginger, originating in South-East Asia, and has been cultivated for thousands of years as a spice and for medical purposes. The aim of this study is to isolate the active principle from extracted essential oil of fresh *Zingiber Zerumbet* rhizomes by steam-hydrodistillation method. In addition, to determine the purity of this active compound using validated reverse phase high performance liquid chromatography (RP-HPLC). Moreover, the antiproliferative effects of this active principal on various human cancerous and noncancerous cell lines at concentrations of 1 to 100 µg/mL were quantified by MTT assay. As a result, colorless zerumbone (ZER) crystals about 1.3 g/kg as an active principal were extracted from the essential oil of fresh *Z. Zerumbet* rhizomes. The purity of ZER crystals were shown to be (99.96%). Simultaneously, ZER exhibited significant ($P < 0.05$) inhibitory effects towards various human cancerous cell lines, while not affected noncancerous cell lines. In conclusion, ZER is suggested to be further developed into a safe therapeutic compound for the treatment of various human cancers.

CARBON NANOMATERIALS AS DRUG TRANSPORTER FOR CANCER THERAPY

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There is a vigorous and growing research effort developing carbon nanotubes (CNTs) for medical applications. It is now known that nanocomposites of Single Wall Nanotubes (SWNTs) can be used to deliver anti-cancer drugs to cells. Also, SWNTs are efficient at converting near infrared (NIR) light to heat, and can do so in a cell, and so cancer cells can be targeted for destruction by NIR radiation, once the cells have taken up SWNTs. SWNTs are highly insoluble in water, but can be functionalized via physical or covalent attachment of solubilizing molecules and drugs of interest. Once this is done, they are readily taken up by cells. We found evidence that our CNT nanocomposites were found to enter cells via endocytosis (the mechanism cells use to take up nutrients); this agrees with earlier work by Dai and coworkers. Herein, we perform systematic study of the internalization, delivery and subcellular localization and possible adverse effects of SWNTs dispersed in culture media and SWNTs wrapped with different fluorescently labelled peptide (FLP-SWNTs) on Chinese hamster ovary (CHO) cells and SWNTs attached with anti-cancer drug on two common cancerous cell lines, human epithelial carcinoma cell line (HeLa) and colorectal cancer cell lines (WiDr).

IN VITRO ANTI-CANCER EFFECT OF LAYERED DOUBLE HYDROXIDE-CHLOROGENIC ACID NANOPARTICLES AS DRUG DELIVERY SYSTEM

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Layered double hydroxides (LDHs) have obtained significant attention as nano-sized carriers for therapeutic and bio-active molecules. LDH nanoparticles are competent for drug delivery purposes due to their numerous advantageous properties such as unique structure, high anionic exchangeability and solubility in acidic media which give rise to the controlled release of intercalated molecules. Hence, the aim of this study is to investigate the properties of newly constructed drug delivery system consisting a natural compound, chlorogenic acid (CA) intercalated into Zn/Al-LDH interlayers for the formation of the nanocomposite. Structural and physical properties of chlorogenic acid intercalated into Zn/Al-LDH (CA-Zn/Al-LDH) were determined by X-ray diffraction, field emission scanning and transmission electron microscope. Loading efficiency of CA in between the interlayers of Zn/Al-LDH was investigated using a UV-Vis spectrophotometer. Subsequently for *in vitro* work, the anti-cancer properties of CA-Zn/Al-LDH nanocomposite on various cancer and normal cell lines were carried out using 3-(4,5-dimethylthiazol 2-yl)-2,5-diphenyl bromide (MTT) reduction assay. Half-maximal inhibitory concentrations of CA-Zn/Al-LDH in all the cell lines was found to be ranged from 0-50 μg/L, determined after 24, 48 and 72 h. To justify their efficacy, apoptosis induction and clonogenic inhibition of chlorogenic acid-LDH nanocomposite were observed and analyzed microscopically. The preliminary result of this study may offer valuable primary information towards the development of potential nanodrugs for cancer therapy.

PROTOCATECHUIC ACID-ZINC/ALUMINIUM LAYERED DOUBLE HYDROXIDE NANOCOMPOSITE AS AN ANTICANCER NANODELIVERY SYSTEM

F. Barahuie, [1], M.Z. Hussein[1], Shafinaz Abd Gani[2,3], Sharida Fakurazi[3,4], Zulkarnain Zainal[1]*

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Protocatechuic acid, an anticancer agent has been intercalated into Zn/Al-layered double hydroxide at Zn to Al molar ratio of 2 using two different preparation methods; co-precipitation and ion-exchange and labeled as PZAE and PZAC, respectively. The release of the anion, protocatechuate from both of the nanocomposites occurred in a controlled manner governed by pseudo-second order kinetics. The basal spacing of resulting nanocomposites PZAE and PZAC was 10.2 and 11.0 Å, respectively, indicating successful intercalation of protocatechuate anions into the interlayer galleries of Zn/Al-LDH in monolayer arrangement with an angle of 24 and 33° from z axis for PZAE and PZAC, respectively. The formation of the nanocomposites was confirmed by Fourier transform infrared study and surface area analysis showed that the nanocomposites are of mesoporous-type material. The thermal stability of the intercalated protocatechuic acid significantly enhanced compared to its counterpart, free protocatechuic acid. The drug loading in the nanocomposites was estimated to be about 32.6% in PZAE and 29.2% in PZAC. Both PZAE and PZAC nanocomposites inhibit the growth of human cervical (HeLa), liver (HepG2) and colorectal (HT29) cancer cell lines and show no toxic effect towards normal fibroblast 3T3 cell after 72 hours of treatment.

CYTOTOXIC PROFILES OF A NANODRUG DELIVERY BASED ON 6-MERCAPTOPURINE-COATED MAGNETITE-PEG NANOPARTICLES TOWARDS LEUKEMIA (WEHI-3B) CELL LINES

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A drug active, 6-mercaptopurine (MP) was coated on the surface of Fe_3O_4-PEG nanoparticles using co-precipitation method in order to form a new magnetic nanocomposite (FPEGMP). The physico-chemical properties of the nanocomposite were studied via X-ray diffraction, infrared spectroscopy, magnetic measurements, thermal analysis and transmission electron microscopy. The resulting superparamagnetic nanocomposite has spherical shape with average particle size diameter of 11 nm. Thermal analyses and Fourier transform infrared (FTIR) spectroscopy revealed the formation of PEG-MP on the surface of iron oxide nanoparticles and the enhancement of the thermal stability of the nanocomposite compared to its counterpart, free 6-mercaptopurine. Release behavior of MP from FPEGMP nanocomposite was found to be sustained and governed by pseudo-second order kinetic. The maximum percentage release of MP from FPEGMP nanocomposite reached about 60% and 97% within approximately 92 and 72 hours when exposed to aqueous solutions at pH 7.4 and pH 4.8, respectively. Anti-cancer activity of the nanocomposite shows that the choice of coating material as well as the percentage of loading of the active agent could affect the cytotoxic activity of nanocomposite towards the mouse myelomonocytic leukemic cell line (WEHI-3B).

IN VIVO ASSESSMENT OF NANOSTRUCTURED LIPID CARRIER FOR ORAL DELIVERY OF ZERUMBONE IN LEUKEMIC MICE MODEL

Heshu, S.R.[1,2,3], Abdullah, R.[1,2], Hemn, H.O.[1,2] , Chartrand, S.M.[4], Ahmad Bustamam, A.[2], Zahra, A.[5], Mahnaz, H.[2], Nozlena, A.S.[2]*

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Cancer nanotherapeutics are progressing rapidly with innovative drug delivery systems to replace conventional delivery systems. Although, antitumor activity of zerumbone (ZER) has been reported, there has been no available information of ZER-loaded nanostructured lipid carrier (NLC) affects murine leukemia cells *in vivo*. In a previous study, ZER was incorporated into NLC by high pressure homogenization (HPH) technique. Physicochemical characterization included particle size, polydipersity index, zeta potential, pH, entrapment efficiency, loading capacity, stability study, and *in vitro* drug release, as well as physicochemical stability after being autoclaved and stored at 4˚C, 25˚C and 40˚C for 1 month, were examined. In this study, *in vivo* effects of ZER-NLC on murine leukemia WEHI-3B cells were investigated. The outcomes of histopathology, TEM and TUNEL assays of BALB/c leukemia mice revealed that the number of leukemia cells were significantly ($P < 0.05$) decreased in spleen tissue after four weeks of oral administration of ZER-NLC. In conclusion, NLC is suggested as a promising carrier for ZER oral delivery.

ANALYSIS OF PERIPHERAL BLOOD OF OVARIAN CANCER PATIENTS INDICATES HIGHER SUB-POPULATIONS OF NATURAL KILLER AND B CELLS COMPARED TO HEALTHY VOLUNTEERS

Tan Jun Hao[1,5], Vicknesh a/l Visvalingam[2], Noor Azmi bin Mat Adenan[4], Norhafizah Mohtaruddin[1], Maha Abdullah[1], Andi Anggeriana[1,2,3]

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Ovarian cancer is a challenging disease to treat, and one of the potential treatments is by immunotherapy. NK cells have been shown to play a role in slowing tumour progression and cancer development. This study aims to investigate the numbers of NK cells and other lymphocyte sub-populations in ovarian cancer and their impact on ovarian cancer clinical outcome. This project aims to study the significance of different lymphocyte populations, particularly NK cells, involved in the peripheral blood of ovarian cancer patients. Venal blood was drawn from ovarian cancer patients before chemotherapy. PBMCs were isolated from 13 ovarian cancer patients and 11 age-matched healthy volunteers. Immunophenotyping was performed using a commercial kit to quantify the lymphocyte populations and RNA isolation performed to examine the expression of KIR genes using reverse transcription polymerase chain reaction. Immunophenotyping of PBMC was successfully performed on 13 ovarian cancer patients and 11 healthy controls. Significant increases in the mean of peripheral NK cells and B cells were found in ovarian cancer patients as compared to the healthy controls (P=0.0559). No other significant results were obtained for C D4 and CD8 lymphocytes. There was significant increase in numbers of NK cells and B cells in ovarian cancer patients as compared to the healthy volunteers. These results should be pursued with a larger sample size with the hopes of finding a significant difference between the two groups and to provide a keener insight into are promising preliminary results the immune defence against ovarian cancer

'A FLY IN THE OINTMENT'

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The small endobronchial malignancies are rare entity that can cause obstruction of the major airways, causing symptoms such as dyspnoea, cough, haemoptysis and postobstructive pneumonia. The obstruction may lead to gradual asphyxiation. Case series of four patients: primary carcinoid, mucoepidermoid carcinoma and mixed squamo-adenocarcinoma are reviewed. This paper describes each of these cases including the clinical presentation, plain film at presentation, CT abnormalities and discusses the utility of CT in their diagnosis. Treatment and progression of disease also will be discussed.

ANTI CANCER ACTIVITY OF MANGIFERIN FROM METHANOL EXTRACT OF FRUIT OF MAHKOTA DEWA (*PHALERIA MACROCARPA (SCHEFF.) BOERL.*)

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Phaleria macrocarpa (Scheff.) Boerl known as Mahkota Dewa is one of Indonesia's traditional medicines from family of *Thymelaeaceae.* Traditional medicine practitioners claim that the chemical compounds in mahkota dewa retains antihistamine, antioxidant and anti cancer effects. In this study, one compound has been successfully isolated from methanolic extract of Mahkota Dewa's fruit as single compound known as mangiferin. To ensure whether this compound; mangiferin contribute to the anti cancer activities, the cytotoxic effect on a breast cancer cell line; MCF-7, cervical cancer cell line; HeLa, and human colon adenocarcinoma cell; HT-29, was examined. The results show that Mahkota Dewa can be promising sources of natural products with potential anti cancer.

CYTOTOXICTY OF ZERUMBONE AGAINST LIVER CANCER CELL LINES (HepG2) VIA APOPTOSIS ACTIVITY

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Zerumbone (ZER), a sesquiterpene phytochemical isolated from a type of edible ginger known as "Zingiber Zerumbet Smith" grown in Southeast Asia. The anticancer effects of ZER has been previously reported at our Laboratory, which used MTT assay on human cancer cells of several cell lines such as cervix (HeLa), leukemia (jurkat) and breast (MCF-7). ZER anti-cancer properties were found to be in equivalent with cisplatin, a commercial anticancer drug used preferentially in treating cervical cancer in humans. In this study, MTT assay was carried to obtain the IC_{50} value of zerumbone towards HepG2 and normal liver, WRL-68 cell lines. The cytotoxicity analysis on HepG2 cells revealed that the IC_{50} is 6.20µg/ml. ZER showed no apparent cytotoxicity response towards WRL-68 cell lines. Morphological analysis for apoptosis detection by using inverted microscope and SEM have produced typical apoptotic characteristic. It showed that zerumbone has antiproliferative activity towards liver cancer cell by its ability to induce apoptosis. The outcome of this study demonstrates that zerumbone has the ability to increased efficacy with limited toxicity in liver cancer treatment.

TOXICITY EFFECT ON DIFFERENT TYPES OF TIGER MILK MUSHROOM EXTRACTS AGAINST HUMAN NORMAL LUNG CELL (MRC5) AND LUNG CANCER CELL (A549)

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Lignosus rhinocerus (Cooke) Ryvarden, also known as the "tiger's milk mushroom", has been traditionally utilised for the treatment of cough, fever, chronic hepatitis, gastric ulcer, liver and breast cancer based on ethnobotanical knowledge. In this study, cultivated tuber of Tiger's Milk Mushroom was dried and grinded to obtain the mushroom powder. Five different types of extract were performed from this mushroom powder. Those crude extracts were petroleum ether (PE) extract, chloroform (CH) extract, methanol (ME) extract, cold water (CW) extract and hot water (HW). The aim of this study is to evaluate toxicity effect on these mushroom extracts against human lung cell (MRC5) and lung cancer cell (A549) through MTT assay. Results showed that IC_{50} of PE, CH, ME and CW were 53µg/ml, 34µg/ml, 56µg/ml and 37µg/ml on MRC5, respectively. The values showed that these four extracts are toxic to MRC5. Only HW extract did not showed 50% inhibition on MRC5 but showed toxicity activity on lung cancer cell (A549) at IC_{50} value of 76 µg/ml. As the conclusion, hot water extract of Tiger's Milk Mushroom can be suggested as not toxic on human lung cell (MRC5) but toxic on lung cancer cell (A549). Fractionation of bioactive compounds from hot water extract of Tiger's Milk Mushroom will be conducted for further study.

CYTOTOXIC EFFECTS OF BIO-SYNTHESIZED ZINC OXIDE NANOPARTICLES ON MURINE CELL LINES

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Zinc oxide nanoparticles (ZnO-NPs) are among the most appropriate metal oxide nanoparticles to exhibit significant potential for treatment properties in a broad spectrum of applications in biomedicine, such as in the treatment of various cancers. The aim of this study was to evaluate the *in vitro* cytotoxic activity and cellular effects of previously prepared ZnO-NPs using brown seaweed (*Sargassum muticum*) aqueous extract. Consequently, *In vitro* anticancer activity was demonstrated in murine cancer cell lines of breast cancer (4T1), lung adenocarcinoma (CRL-1451), colon cancer (CT-26), and acute myelocytic leukemia (WEHI-3). Treated cancer cells with ZnO-NPs for 72 hours demonstrated various levels of cytotoxicity based on calculated IC_{50} values using MTT assay as follows: 21.7 ± 1.3 µg /mL (4T1), 17.45 ± 1.1 µg /mL (CRL-1451), 11.75 ± 0.8 µg /mL (CT-26) and 5.6 ± 0.55 µg /mL (WEHI-3), respectively. On the other hand, ZnO-NPs treatments for 72 hours showed no toxicity against normal mouse fibroblast (3T3) cell lines. Furthermore, distinct morphological changes were found by utilizing flourescent dyes, as apoptotic population were increased via flowcytometry, while cell cycle block and stimulation of apoptotic proteins were also observed. Additionally, the present study showed that the caspase activations contributed to ZnO-NPs triggered apoptotic death in WEHI-3 cells. Thus, the nature of biosynthesis and the therapeutic potential of ZnO-NPs could prepare the way for further research on the design of green synthesis therapeutic agents, particularly in nanomedicine, for the treatment of cancer.

EFFECTS OF GOLD NANOPARTICLES SYNTHESIZED USING WATER EXTRACT OF BROWN SEAWEED; SARGASSUM GLAUCESCENS

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Based on data published in April 2011 by WHO about Deaths in worldwide, cancer is the third leading cause of death (after heart disease and stroke) in most of developed countries and the second leading cause of death (after heart disease) in Malaysia . Therefore, one of the challenges for Malaysia and the whole world is carrying out research on cancer in order to find its causes and method for therapy and prevention of this disease. Metal nanoparticle synthesis using seaweed extract shows rapid and non-toxic process which resulted to nano sizes having the greatest potential for biomedical applications. The current study was aimed to investigate the anticancer properties of gold nanoparticles synthesized using water extract of brown seaweed; *Sargassum glaucescens*(Au/S.G-NPs). The effect of 3.65±1.69 nm Au/S.G-NPs were studied on HeLa (cervical cancer) and 3T3 (mouse fibroblast) using tetrazolium dye MTT assay. Later on, *in vitro* apoptosis effect was evaluated using fluorescent microscopy, flow cytometry, and protease caspase activities. After 72 h treatment , MTT assay revealed highest and significant cytotoxic effect of Au/S.G-NPs dose and time-dependently against cervical cancer cells with IC_{50} of 4.75 ± 1.23 µg/mL. On the other hand, Au/S.G-NPs showed no cytotoxic effect toward mouse fibroblast cells. Moreover, Au/S.G-NPs significantly *($P < 0.05$)* arrests HeLa cells at G2/M phase and significantly *($P < 0.05$)* activated caspases-3 and -9. The results revealed that Au/S.G-NPs can be further developed as chemotherapeutic compound for the treatment of cancers especially cervical cancer.

LINKAGE ANALYSIS BETWEEN PROSTATE CANCER OCCURRENCE AND Y-CHROMOSOMAL DYS LOCI IN MALAYSIAN MALE SUBJECTS

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Prostate cancer has become the second leading cancer among men across ethnic groups in the world. Since it is influenced by a complex genetics that may affect the level of susceptibility for the development of the disease, four Y-linked short tandem repeats (STRs), DYS388, DYS435, DYS437, and DYS439 were genotyped to compare Malaysian prostate cancer patients and normal controls males. A total of 175 subjects comprising 84 patients and 91 healthy individuals from three major ethnics were recruited. Multiplex PCR was optimized to co-amplify all four DYS loci. All samples were genotyped for alleles of four DYS loci using a Genetic Analysis System. Result showed that allele 10 (A) of DYS388 had a significantly lower incidence towards disease than other alleles of this locus, while allele 12 (C) of DYS388 and allele 14 (E) of DYS439 showed a significantly higher risk to develop prostate cancer compared to other alleles of these loci. Moreover, among 47 different haplotypes comprising different alleles of four DYS loci found in the overall study samples, it is noticed that AABC and CAAA showed a lower and higher frequency among cases than controls, respectively. As a conclusion, Malaysian males who belong to Y-lineages with either allele 12 of DYS388, allele 14 of DYS439, or haplotype CAAA tend to develop prostate cancer. Meanwhile, those belonging to Y-lineages with allele 10 of DYS388 or haplotype AABC are more resistant to the disease. Thus, it is suggested that genetic elements give an influence on the development of prostate cancer.

MIR-137-MEDIATED LOSS OF KDM5B EXPRESSION LEADS TO SUPPRESSION OF THE MALIGNANT PHENOTYPE OF BLADDER CANCER CELLS

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The oncogenic role of KDM5B is implicated in the pathogenesis of many cancers including bladder cancer (BC). KDM5B is a histone demethylase enzyme that modifies the chromatin structure to specify cellular transcriptional states. Overexpression of KDM5B in cancer cells is correlated with an increased proliferative capacity. Intriguingly, KDM5B is a cancer/testis antigen; while its expression in tumours is ectopically amplified, KDM5B expression in normal conditions is limited to embryonic stem cells (ESCs) and the testis in adults. These unique characteristics make KDM5B a potential pan-cancer therapeutic target. Thus, this study was aimed at identifying potential regulators of KDM5B. Since KDM5B expression in ESCs is orchestrated by microRNAs (miRNAs) and the expression of many miRNAs are altered in BC, we hypothesized that miRNAs may be the switch that can abate KDM5B expression to mitigate the BC malignant phenotype. Based on IHC- and RT-QPCR analysis, we found that KDM5B protein and transcript levels were differentially expressed in cancer tissues and cell lines, respectively. Amongst several *in silico*-predicted putative KDM5B-targeting miRNAs, the *in vitro* basal expression of miR-137 was inversely correlated with KDM5B expression. We demonstrated that the overexpression of miR-137 significantly attenuated KDM5B expression, induced G1 cell-cycle arrest, suppressed cell growth and blocked invasion and migration of BC cells. In contrast, downregulation of miR-137 expression led to the reverse effect. By integrating *in silico* screens of miR-137 putative target genes and microarray data using the Ingenuity Pathway Analysis (IPA), we revealed that miR-137 possibly exerts control over the cell-cycle through Rb and adenylyl cyclic signalling pathways by targeting key regulators of cyclin A. We also showed that miR-137 gain-of-function increased the expression of tumor suppressor, JDP2. While our results suggest that miR-137 can mitigate the KDM5B-associated BC phenotype, further studies on understanding the effect on aberrant histone methylation patterns are warranted.

BACTERIA AS POTENTIAL TUMOUR FIGHTER

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Despite significant progress in the development of therapeutic drugs and treatments, deaths due to cancer still remains high. These therapies are also not specific to tumour regions, hence causing adverse effects to the patients. Bacteria had long been studied for its ability to multiple within tumour regions and also reducing tumour volumes. *Salmonella* had also been studied and shown to be able to attack cancerous cells. To ensure the bacteria therapy is safe for clinical trial purposes, the bacteria need to undergo the process of silencing and *in vivo* assessment. This study was carried out to assess the use of SPI knockout *S.* Typhimurium and *S.* Agona as a possible tumour reduction agent and to investigate the effect of the SPI knockout strains on the survival of mice with induced tumour. 3 x 10^6 CT26 cells suspended in PBS were inoculated subcutaneously on the thigh to induce solid tumour. The subjects were then treated with the four bacterial treatments via intraperitoneal and intratumoural route of administration. The changes in the sizes of the tumours were observed daily using a calipher. The subjects were then sacrificed and the organs were harvested for histopathological analysis. One-way ANOVA indicated that the treatments had significant effects at $p < 0.05$, on both the changes of the tumour volumes and also the survival periods of the subjects. Subjects treated with *S.* Agona showed better survival compared to subjects treated with *S.* Typhimurium. *S.* Agona is found to be a better candidate as a tumour reduction agent, compared to *S.* Typhimurium, since it showed longer survival period of subjects after treatment and yet, had similar capacity as a tumour reduction agent.

CANINE MAMMARY GLAND TUMOURS DIAGNOSED AT VETERINARY HISTOPATHOLOGY LABORATORY, FACULTY OF VETERINARY MEDICINE, UNIVERSITI PUTRA MALAYSIA 2006 – 2012

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Dogs develop neoplasia naturally and spontaneously just like in humans. Mammary gland tumour is the most common neoplasm in female dogs. Age of dog, neuter status, breed size and pedigree have all been described to significantly affect the risk of canine mammary gland tumour (CMT) development. This study aimed to determine the prevalence of CMT diagnosed at the Veterinary Histopathology Laboratory, Faculty of Veterinary Medicine, University Putra Malaysia, between 2006 and 2012 and to evaluate the proportion of breed types, neuter status and age on the odds of CMT development. Forty-eight cases with confirmed diagnosis of CMT on histopathology were reviewed retrospectively. Thirty-nine (81.25%) were diagnosed as adenocarcinoma and 8.33% (n=4) for each squamous cell carcinoma and mixed cell tumour respectively. Adenoma was only diagnosed in one CMT. The prevalence of CMT in this study is 39%. When CMT cases were compared with all other diagnosis in dogs, CMT was significantly more in adult dogs (p=0.032, logistic regression 0.012) and intact dogs (p=0.009, logistic regression, (0.003). When CMT cases were compared with other types of neoplasia, significant association with CMT was observed in pure breeds (p=0.025) and intact dogs (p=0.000034, logistic regression 0.00042). This study found that pure breed dogs, intact dogs and older dogs (>5years) have higher odds of having CMT.

OVEREXPRESSION OF CTAG1B IS A POTENTIAL BIOMARKER IN BLADDER CANCER

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Urothelial cell carcinoma (UCC) is the most common form of bladder cancer and is associated with the need for life-long surveillance once a patient is diagnosed with a non-invasive disease. Due to the long-term risk of recurrence and the need for life-long routine monitoring and therapy, the cost per UCC patient from diagnosis to death is the highest of all cancers. The development of non-invasive biomarkers of recurrence and progression can increase survival, decrease treatment costs and improve patient quality of life. However, to date, no biomarker(s) have been endorsed for the use in the clinical management of UCC, especially in predicting risk of progression and recurrence. CTAG1B was previously found to be highly expressed in high-stage and grade bladder cancer, albeit in Caucasian cohorts. However, despite its potential as a target for cancer immunotherapy, the effect of expression modulation on cellular phenotypes has never been reported. In this study, we overexpressed CTAG1B in an invasive bladder cancer cell line, EJ28 after we confirmed that this cell line minimally expressed CTAG1B. The cells were transfected with CTAG1B-pcDNA3.1(-) and the level of expression was confirmed by qRT-PCR. Once the expression was confirmed to persist up to 72h post-transfection, the transfected cells were subjected to various phenotypic assays. In addition, the pattern of CTAG1B expression in a cohort of Malaysian bladder cancer paraffin-embedded tissues was also determined using immunohistochemistry. The effect of CTAG1B overexpression on the cell cycle, migratory and proliferative potential was observed. The changes in phenotype were compared with that of untransfected and mock controls. CTAG1B was overexpressed 20 times as compared to the untransfected and mock controls in the transfected cells. CTAG1B overexpression resulted in cells to migrate slower at 24h post-transfection but proliferate significantly faster after 72-96h post-transfection. In addition, CTAG1B was more frequently expressed in advanced bladder cancer stages and grades. The findings from this study contribute to the current knowledge of CTAG1B's role in tumourigenesis. Further functional studies will contribute towards realising the potential of CTAG1B as a biomarker for predicting the risk of progression and recurrence of bladder cancer.

FIBROBLAST GROWTH FACTOR RECEPTORS: THEIR EXPRESSION AND CLINICOPATHOLOGICAL RELEVANCE IN CANINE MAMMARY GLAND TUMOURS

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Mammary gland tumour (CMT) is the most common neoplasm which occurs naturally in dogs. CMT affects mainly female dogs and can lead to metastatic disease and eventually death if untreated. Among the recent biomarkers involved in growth signaling explored in human cancers which are yet to be explored in canine mammary gland tumours are the fibroblast growth factor receptors. This study aimed to determine the expression of FGFRs in CMT and the relationship between the expression and clinicopathological parameters. Forty-six CMT were immunohistochemically probed for the expression of FGFR2, FGFR3 and FGFR4 using rabbit polyclonal antibodies. Western blotting was used to evaluate cross reactivity of the antibodies with the canine FGFR protein. The expression of FGFR2 was significantly associated with histopathology grade 3 of the tumours p=0.027. FGFR4 expression was associated with large breed dogs p=0.044, and large tumour size (>3cm), p=0.045. Many studies in human cancers have reported prognostic value of FGFR expression. FGFR2 expression was associated with histopathology grade, indicating the usefulness of high FGFR2 expression in CMT as an indicator of increased tumour malignancy. Large tumours have shown significantly higher FGFR4 expression. Tumour size is one of the criteria for tumour staging (TNM), which placed large tumours (>3cm) on stages 2 and above. Large breed dogs have a significantly higher FGFR4 expression in this study. Based on these findings, FGFR2 and 4 can be used as markers for advanced and aggressive CMT which further studies are warranted to evaluate for possible targeted therapy.

THE CYTOTOXCITY ACTIVITY OF *IN VITRO* ISOLATED AND EXPANDED CYTOTOXIC T-LYMPHOCYTES AND NATURAL KILLER CELLS IN BLADDER CANCER

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The expanding roles of the immune system in tumourigenesis have established immunotherapy as a potential mainstream cancer therapeutic modality. *Ex vivo* expanded and activated cytotoxic T-lymphocytes (CTLs) and natural killer (NK) cells have been found to be efficacious in the treatment of various types of cancers. One of the biggest limitations is the ability to generate and store cytotoxic immune cells in larger numbers without losing its cytotoxicity. Consequently, we evaluated the *in vitro* cytotoxic activity of freshly cultured and cryopreserved CTLs and NK cells that were expanded *in vitro*. We also compared the synergistic cytotoxic activity of CTLs and NK cells in combination. The cytotoxic activity was measured in bladder cancer cell lines, EJ28 (invasive) and RT112 (minimally-invasive). All experiments were run in three replicates. The cellular phenotype of the isolated and expanded effector cells was characterised using flow cytometry. MTT assay was performed to assess the dose- and time-dependent cell-mediated cytotoxic activity in the bladder cancer cells. An effector to target ratio of 1:1, 2:1, 5:1, 10:1 and 20:1 was tested after 4 h, 12 h and 24 h incubation. The fresh *in vitro* expanded effector cells had a high percentage of cell viability and expressed cytotoxic markers CD8+ and CD56+ in the CTL and NK cell cultures, respectively. Although the expansion capacity of the cryopreserved cells was limited, the expression of the functional markers and cytotoxic activity of these effector cells were maintained. All the effector cells exhibited significant cytotoxic activity at the effector to target ratio of 5:1 at 4 hours of co-culture. This was confirmed through the real-time observation of the morphological changes of the cells using an inverted phase contrast and time-lapse confocal microscope. The *ex vivo* generated CTLs and NK cells appear to retain their functionality, especially in recognizing their allogeneic target and thus, serve as a foundation to build on for future therapeutic applications. .

THE DESIGN OF RESTORATIVE OUTDOOR ENVIRONMENTS FOR CANCER PATIENTS

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A cancer diagnosis brings with it multiple psychological crises, including loss of control, loss of self-efficacy, isolation, decrease self-esteem and, grief. Several studies have presented evidences that actual or stimulated view of nature can produce substantial restoration from psychological stress within a few minutes. A research also found that patients recovered faster and with fewer strong medications when windows faced a natural view rather than a brick wall. This paper will discuss how outdoor spaces with restorative qualities may provide an environment conducive to stress reduction, mental repose, emotional recovery and, the enhancement of mental and physical energy. Literature concerning the design recommendations for outdoor environments for cancer patients are identified and analysed. Among the design considerations include implementing interactive garden features, spaces for different type of users (adult, children, staff and visitors) and, easy access. A case study using Post Occupancy Evaluation at the National Cancer Institute in Malaysia is being carried out in order to investigate the possibilities of having a restorative outdoor environment in a local context. The knowledge gathered from this study may contribute to the body of knowledge in designing outdoor environments for cancer treatment centres in Malaysia.

O-CARECLOUD: OVARIAN CANCER PATIENT MANAGEMENT SYSTEM ON CLOUD

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Ovarian cancer is the fifth common cancer among Malaysian women from all ethnicities. Ovarian cancer is not easy to detect early. Often women with ovarian cancer have no symptoms or show mild and non-specific symptoms, until the disease has reached an advanced stage. Researchers are exploring ways to improve the early detection of ovarian cancer. This includes exploring the usefulness of a trans-vaginal ultrasound, and of measuring levels of CA-125, a tumor marker that is often found in higher than normal amounts in the blood of women with ovarian cancer. In an effort to improve the quality of healthcare delivery to cancer patients, O-CareCloud for patient management system on cloud is providing the online availability of ovarian cancer patient's health record, to retrieve and storage data and management. This system is for department O&G of Hospital Serdang focusing on ovarian patient. The scope of our system focus on helping the doctors to access and diagnose the tumour from an ultrasound examination which the doctors can differentiate a fluid filled cyst, solid tumour masses and healthy tissues. Second the system identify by using the result of CA-125 Assay blood test which is to measure the level of CA-125, a tumour marker, in the blood. The system can be accessed by doctors in charged portably meaning anywhere and anytime.

RANDOM WALKERS BASED BREAST THERMOGRAPHY IMAGE SEGMENTATION

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The leading cancer diagnosed in woman in Malaysia and Asia Pacific region is the breast cancer. With the introduction of standardized image interpretation criterion and the increase in computational capacity coupled with the renewed interest from the medical community, breast thermography is now being considered as an adjacent to the mammography. The lack of any ionizing radiation makes thermography an ideal method for initial screening of young women, also the chemotherapy progress can be easily monitored by thermography while other methods such as mammography cannot be used due to the caused radiation. Despite the fact that computer aided detection/diagnosis (CAD) of breast thermography has become highly accurate, Image segmentation methods for breast thermography remained at a moderately accuracy, while the basis for any good CAD system is a proper segmentation. To address this issue a new framework based on random walkers were developed to segment breasts in thermography images. In breast thermography diagnostic, proper detection and segmentation of the breast boundaries present the biggest challenge. As the boundaries of breasts, especially in the upper quadrants, are usually not present, this produces a great deal of challenge to segment breasts automatically. Many approaches have been developed to segment the breast in thermography such as Snakes, Active Contours and Circular Hough Transforms, but most of these methods fail to detect the boundaries of the breast with the required level of accuracy especially the upper boundaries of the breast, while most of them require the image to be manually adjusted and cropped to ensure proper segmentation. By utilizing random walkers, the breast can be segmented accurately and automatically which in turn will increase the accuracy and the reliability of human interpretation and/or computer aided detection/diagnosis systems.

COMPUTER AIDED DETECTION/DIAGNISIS FOR BREAST CANCER DETECTION IN COMPUTED TOMOGRAPHY LASER MAMMOGRAPHY (CTLM)

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Breast cancer is the leading cancer killer among women. Early detection and new treatments have improved survival rates. Although mammography is the gold standard for breast cancer screening, increasing awareness indicate that there is some limitation for part of women whom mammography reduce sensitivity based on their breast density. Other modalities such as ultrasound and magnetic resonance imaging and recently computed tomography laser mammography (CTLM) are often suggested as an adjunct to mammography to achieve additional information and increase sensitivity. The angiogenesis is known a critical for tumor growth and spread of breast cancers. Computed tomography laser mammography (CTLM) CTLM has been introduced to verify angiogenesis at early stage. In this modality, there are no restriction factors such as age or breast density. Main difficulty for radiologists is closeness of color shade to interpret CTLM images. Computer-aided detection /diagnosis (CAD) systems have been developed to help radiologists in order to increase diagnosis accuracy. Generally, a CAD system consists of four stages: (a) pre-processing, (b) segmentation of regions of interest, (c) feature extraction and selection, and finally (d) classification. The aim of this research is to develop a CAD system in computed tomography laser mammography (CTLM) to detect and classify benign and malignant lesions in the breast. .

AN INTEGRATIVE CANCER CLASSIFICATION BASED ON GENE EXPRESSION DATA

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The advent of integrative approach has shifted cancer classification task from purely data-centric to incorporate prior biological knowledge. Integrative analysis of gene expression data with multiple biological sources is viewed as a promising approach to classify and to reveal relevant cancer-specific biomarker genes. The identification of biomarker genes can be used as a powerful tool for understanding the complex biological mechanisms, and also for diagnosing and treatment of cancer diseases. However, most integrative-based classifiers only incorporate a single type of biological knowledge with gene expression data within the same analysis. For instance, gene expression data is normally integrated with functional ontology, metabolic pathways, or protein-protein interaction networks, where they are then analysed separately and not simultaneously. Apart from that, current methods generates a large number of candidate genes, which still require further experiments and testing to identify the potential biomarker genes. Hence, this study aims to resolve the problems by proposing a systematic integrative framework for cancer gene expression analysis to the classification task. The association based framework is capable to integrate and analyse multiple prior biological sources simultaneously. Set of biomarker genes that are relevant to the cancer diseases of interest are identified in order to improve classification performance and its interpretability. In this paper, the proposed approach is tested on a breast cancer microarray dataset and integrated with protein interaction and metabolic pathway data. The results shows that the classification accuracy improved if both protein and pathways information are integrated into the microarray data analysis.


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