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# INTERNATIONAL CONFERENCE OF MOLECULAR MEDICINE IN NUTRITION, HEALTH AND DISEASE 16-17 APRIL 2018

## 'EMBRACING FRONTIERS OF MOLECULAR MEDICINE IN NUTRITION, HEALTH AND DISEASE'

## CONCORDE HOTEL, SHAH ALAM SELANGOR MALAYSIA

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# KEYNOTE LECTURE

## EMBRACING FRONTIERS OF MOLECULAR MEDICINE IN NUTRITION, HEALTH AND DISEASE

***Nora O'Brien***
*School of Food and Nutritional Sciences, University College Cork, Ireland*

Major transitions have occurred over the past two centuries in world demographics and epidemiological patterns of disease as different countries have undergone economic development at varying rates. The poorest countries still tend to have higher fertility rates and predominantly younger population age profile. Economic development typically leads to lower fertility rates and aging population. Additionally, the poorest countries still experience large prevalence of infectious diseases as causes of mortality whereas the more economically developed nations have transitioned to mainly non-infectious chronic diseases. These demographic and epidemiological transitions typically precede the nutrition transition, i.e., the poorest countries have very significant prevalence of undernutrition and the most developed countries very significant levels of overnutrition which is most clearly manifested by rising levels of obesity. As this century progresses, overnutrition and obesity will become the most significant public health nutrition issue worldwide. A large evidence base has been generated over the years on the relationship between nutrition and health, both between undernutrition and susceptibility to infectious diseases and also between overnutrition and risk of chronic non-infectious diseases. This evidence base has been generated using a variety of research approaches including epidemiological studies in human populations, animal research studies, and molecular nutrition research. The latter research has traditionally emphasised a nutritional biochemistry approach to understand mechanisms involved at cellular and molecular levels in the role of nutrition and dietary patterns in human disease. In recent times, new and exciting molecular nutrition research techniques (omic technologies) have been increasingly exploited to strengthen the evidence base that underpins food-based dietary guidelines on healthy eating patterns to decrease risk of chronic diseases. The presentation will provide an overview of our understanding of the relationships between nutrition, health and disease in a rapidly changing world and the role of molecular nutrition research in current understanding.

# PLENARY

## OMICS AND VITAMIN E SUPPLEMENTATION: FROM MECHANISMS TO FUNCTION

***Wan Zurinah Wan Ngah***
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The discussion on the benefits or harm of vitamin E supplementation continues although the vitamin E industry is worth billions worldwide. This is further complicated by the presence of different isomers of vitamin E with potentially different properties and biological functions. Interpretation of human supplementation studies need to consider obvious factors such as type of disease or condition of subjects, type of vitamin E used and duration of supplementation. Other important factors not usually considered but have been shown to affect the outcome includes the age of the subjects, population used, presence of oxidative stress such as smoking, gender and nutritional status. However, if the mechanism of action of the effects of vitamin E supplementation is known, some of these factors can perhaps be explained. Research using the omics platform have potential to help elucidate some of the mechanisms involved. In theory, this can clarify the action of vitamin E and perhaps differentiate the different isomers. Our findings using palm oil tocotrienols in animal models and cell lines have shown protective effects in various cancers and ageing. In human supplementation studies, proteomics of plasma showed a decrease in inflammation protein CRP. Differential gene expression studies comparing tocotrienols and tocopherol supplementation revealed differences suggesting the different effects of different vitamin E isomers. The implication of these findings needs further investigation.

## FUNCTIONAL FOOD IN HEALTH AND DISEASE

***Nora O'Brien***
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The concept that health and disease is influenced by nutrition is underpinned by an extensive evidence-base. Traditionally, expert groups have published advice in the form of food-based dietary guidelines on healthy eating patterns. Typically, these guidelines encourage energy balance, consumption of a wide variety of foods with emphasis on plant food sources, and minimizing intake of energy-dense foods high in added sugars, fats and salt. In recent years, an additional approach promoted by sections of the food industry has been the development of functional foods. These foods are marketed as providing specific health benefits beyond basic nutrition. Normally, they incorporate a bioactive ingredient(s) with purported health benefits. Many different bioactive compounds isolated from foods, food waste sources, or other natural sources have been investigated including plant sterols, pre- and probiotics, food peptides, omega-3 fatty acids, dietary fibre components, plant phenolics and carotenoids. Regulatory agencies worldwide have responded to the proliferation of functional foods by strengthening regulations on the evidence-base required for health claims. The relevant bioactive compounds in the functional food have to be characterised, their bioactivity and bioavailability established, and evidence provided demonstrating benefits on physiological function or a validated biomarker of a specific disease in human intervention trials. An overview will be presented of the extensive EU regulations related to the marketing of functional foods with associated nutrition and health claims. Only a small minority of health

claims for functional foods have been approved by the EU to-date. This conservative regulatory approach is supported by the majority of independent public health professionals as health claims need to be accurate and substantiated. While the functional food sector is projected to grow significantly worldwide, the traditional approach involving food-based dietary guidelines on healthy eating patterns is likely to enjoy continued support by the nutrition and public health community.

## UNDERSTANDING THE IMPACT OF INTERACTION BETWEEN GENE AND NUTRIENTS IN HEALTH

***Nor Fadilah Rajab,*** *Elham Pirabasi, Lai Kuan Lee, Razinah Sharif, Suzana Shahar*
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Nutrition has a predominant role in many type of health condition and management. Nutrigenomics is research focusing on finding and understanding at the molecular-level, the interaction between nutrients and other dietary bioactive with the genome. This will lead to an increased understanding on how nutrition influences pathways and homeostatic control and ultimately allow effective dietary-intervention strategies to recover normal homeostasis and prevent diet-related diseases. There is much evidence to support that nutrients may increase genetic stability via repairing damage to DNA. Three different resources of nutrients, namely polyphenols, honey and LCFA, will be presented to clarify the basic knowledge on the interaction between various nutrients and genes in different conditions and diseases. It highlights the important understanding of the interactions between gene and nutrients especially on preventing diseases and promoting health.

## GENE x ENVIRONMENT INTERACTION TOWARDS PREVENTION OF CARDIOVASCULAR DISEASE

***Yap Roseline Wai Kuan***
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Cardiovascular disease (CVD) is still the number one killer worldwide for chronic non-communicable diseases (NCDs). The etiology of NCDs/CVD involves a complex relationship of several risk factors categorised as non-modifiable, modifiable and metabolic factors. Genetics is one of the non-modifiable factors indicating susceptibility to disease risk while modifiable risks are usually environment-related or lifestyle practices such as diet and physical activity. Metabolic risk factors of NCDs/CVD on the other hand include overweight/obesity, hypertension, hyperglycaemia and hyperlipidaemia. Hence, it is crucial to investigate the interplay of these risk factors, which then led to the birth of gene-environment (G x E) interactions research on chronic diseases. The investigation using G x E interactions can account for 'missing heritability', therefore it may serve as a powerful method in the prevention and management of chronic NCDs including CVD.
This presentation will review the most recent studies focusing on gene-diet interaction effects on CVD and its risk factors as diet is the most common environmental factor. The candidate genes related to CVD which have been investigated in these recent literatures include apolipoprotein E (ApoE), cyclin-dependent kinase inhibitor 2A/B (CDKN2A/B), heat shock protein (HSP70), and lipoprotein lipase (LPL). The dietary component was evaluated either based on total energy, total fat or types of dietary fat. This presentation will also include

gene-diet interactions studies on metabolic risk factors of CVD involving Malaysian population. In these studies, the diet component was based on constructed dietary patterns. The selected candidate genes with related polymorphisms include rs1870377 and rs2071559 of vascular endothelial growth factor-2 (*VEGFR-2*) gene, rs5186 of angiotensin II type 1 receptor (*AGTR1*) gene and rs1403543 of angiotensin II type 1 receptor (*AGTR1*) gene. Finally this presentation will end with future recommendations on G x E interactions research on NCDs/CVD in the country and globally to address research gaps.

## STEM CELL THERAPIES FOR MUSCULOSKELETAL DISEASES: CURRENT STATUS, TRENDS, OPPORTUNITIES AND REGULATORY RESTRICTIONS

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Stem cells therapies using mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs) for musculoskeletal diseases has gained worldwide interest owing to its potential regenerative ability. Its use promises reduced morbidity and improved clinical outcomes for many types of diseases, which were previously undertreated. The use of stem cells together with supporting devices and adjunct therapeutics, such as biomaterial, scaffolds and bioreactors, provides potentially viable treatment options that mimic the in vivo environment of the treated native tissue. Despite having seen encouraging results for almost 3 decades, these therapeutic techniques known to many as tissue engineering and regenerative medicine have not been widely employed. For example, in the area of cartilage regeneration, since the first 3 published papers appeared in Medline in 1981 there have been over 6354 articles published to date with over 607 articles published in this area in 2017 alone. However, there are fewer than 24 documented clinical trials published in this area (involving knees), and not one is on the approved U.S. FDA list of cellular and gene therapy products. In fact, of the 17 products approved under this list, only the autologous chondrocyte has been recognized as an accepted therapeutic method and is the only one indicated for musculoskeletal disease. One might ask, why is there a delay in the progress of clinical application? The reason to this is multifold and ranges from poor public perception, low commercial viability to stringent regulatory controls. For example, to date, public concerns with regards to the potential mutation of stem cells and the possibility of these cells to turn malignant remains high on their list. Due to this, local drug administrative authorities such as Malaysia's National Pharmaceutical Regulatory Authority (NPRA) has established many steps and protocols that needs to be met before a product can be authorized for registration. Mirroring other international authorities such as FDA and EMA which regulates stem cell use under Public health legislation and Pharmaceutical legislations, NPRA has established a Cell and Gene Therapy Product Guidelines (GCTP) that is indirectly pegged to the Poison, and Sales of Drug Act 1952. In this guideline, the requirements for registration are stringent and lists down all that is needed to comply. This includes pre-clinical safety checks, GLP and GMP requirements and dossiers of clinical trials. Arguments have arisen from having done this; namely on the cost implication and time to completion of product development. More so when we consider that the present financial and industrial support in this country (with over 90% of the industry is of SMEs) is not sufficiently conducive to progress or even support this area of research in the long term.

Nevertheless, all is not loss and that as a nation that is moving towards becoming a developed nation; such issues should be viewed as merely "inconveniences" that we need to overcome. To move forward from this, it is important that research in this area must take into

account present and future research policies, and of the supporting atmosphere so as to ensure that our efforts remain valid and viable. In this lecture, we will review present policies, trends and the ecosystem that supports this area of research. We will also discuss the efforts that are being made in our attempt to prepare us for the future.

# SYMPOSIUM

# THEME I: APPLICATIONS OF MOLECULAR MEDICINE IN NUTRITION, HEALTH AND DISEASE

## METABOLOMICS AND THE SEARCH FOR BIOMARKERS IN COLORECTAL CANCER

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Metabolomics has been used to identify differentiating metabolites and altered pathways in various types on cancer. The search for biomarkers in colorectal cancer is spurred by the lack of accurate non invasive tools for its diagnosis. The elucidations of affected pathways lead to the understanding of its pathophysiology and hence better prognosis. Serum and plasma are the most common samples analysed apart from tissues, urine and faeces. While serum and plasma are used mainly to determine biomarkers, tissues and even faeces have been used for staging biomarkers as well as to understand its development and progression. Sample preparation, analytical platforms as well as data analysis vary which resulted in different metabolites identified by the different studies. This is further confounded by the biological variations in different studies. Thus there is a need for standardisation to enable specific and sensitive biomarkers to be identified, which can be used across different population.

## THE USE OF PHYTOCHEMICALS IN THE PREVENTION OF ADVANCED GLYCATION END PRODUCTS FORMATION AND ASSOCIATED BONE LOSS

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Prolonged periods of hyperglycemia increase the formation of advanced glycation endproducts (AGE). The accumulation of these non-enzymatically glycated proteins, lipids or nucleotides leads to cellular dysfunction and cell death. AGE tend to accumulate especially in the extracellular matrix of tendons, skin, cartilage and bone leading to a deterioration of the mechanical properties of these tissues and an increased risk of damage and fractures. Therefore we wanted to investigate the effect of AGE on osteoblast cells and if phytochemicals like berberine and genistein could prevent or reduce the formation of AGE and its cellular consequences. Human fetal osteoblast (hFOB 1.19) cells were incubated for 24h with 150 µM methylglyoxal (MG) with and without metformin, berberine, genistein or the

combinations. The expression of AGE, ROS production, DNA damage, cell viability and the changes in expression of bone markers were examined. For all experiments, a minimum of three biological replicates was used and the data were analyzed using ANOVA followed by post-hoc analysis. Incubation of hFOB 1.19 with MG significantly reduced osteoblast cell viability and increased DNA damage, apoptosis, ROS and NO production. A shift in the ratio of osteoprotegerin (OPG) to RANKL towards OPG indicated inhibition of osteoclastogenesis while a decreased expression of OPN and ALP were indicative of inhibited osteoblast cell differentiation and function. Metformin, berberine, genistein and the combinations significantly improved the measured parameters. However, when comparing the treatments, metformin was more potent than berberine, genistein or the combinations in reversing the MG-induced changes. No synergistic effect between metformin, berberine or genistein was observed. In conclusion, MG inhibits osteoblast viability and functions as well as osteoclastogenesis leading to impaired bone remodeling. Although protective, the use of antioxidants is not sufficient to inhibit bone loss.

## VITAMIN E: ITS MOLECULAR MECHANISM IN DELAYING CELLULAR AGEING

***Suzana Makpol***
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The *in vitro* ageing of human diploid fibroblasts (HDFs) is the experimental model for cellular ageing. Human diploid fibroblasts have a limited ability to divide when cultured *in vitro* and will enter a state of cellular senescence. Cellular senescence is the terminal phase of passaged primary human cell population, a response more accurately defined as replicative senescence. One of the most important mechanisms responsible for replicative senescence is cell growth arrest. Senescent cells also show the characteristic of enlarged and flattened morphology, express senescence-associated β-galactosidase, with altered gene expression. In this study we identified the molecular changes that occur with senescence in HDFs and its modulation by palm tocotrienol in delaying cellular senescence. Primary culture of HDFs obtained from circumcision foreskin of 8-12 year-old boys was cultured until senescent. Treatment with tocotrienol was carried out to evaluate its molecular effects on cellular ageing. Our results showed that when cells aged, there were changes in cells morphology, decreased in telomere length and telomerase activity, increased senescence-associated β-galactosidase activity, altered gene expression pattern and changes in cell cycle profile. Treatment with tocotrienol protects against cellular ageing by restoring telomere length and telomerase activity, reducing damaged DNA, and reversing cell cycle arrest associated with cellular ageing. Tocotrienol modulated the expression of *COL I* and *COL III* genes and increased the rate of total collagen synthesis. The expression of ELN and COL1A1 genes were upregulated while MMP1 and IL6 expression was down regulated. Tocotrienol was also found to inhibit apoptosis by modulating the upstream apoptosis cascade, causing the inhibition of cytochrome *c* release from the mitochondria with concomitant suppression of caspase-9 and caspase-3 activation. Microarray data from the Gene Set Enrichment Analysis (GSEA) revealed that tocotrienol modulated biological processes in senescent HDFs such as negative regulation of tumor necrosis factor production and negative regulation of interleukin-6 production (*IRAK3* dan *SelS*), cell redox homeostasis process (*SelS and GLRX5*), negative regulation of caspase activity and response to stress (*HSPA5 and HERPUD1*), endoplasmic reticulum unfolded protein response (*SelS* and *HERPUD1*) and protein transport (ARF). In conclusion, palm tocotrienol may delay cellular ageing of HDFs by modulating gene expression pattern and regulating cell cycle progression.

## GASTROINTESTINAL EFFECTS OF CANCER THERAPY: ROLE FOR NUTRITION

***Joanne Bowen***
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Cancer therapies are diverse and have varied impacts on the gastrointestinal (GI) tract. Traditional regimens of chemotherapy and radiation have been associated with high rates of mucosal injury affecting sites including the oral cavity, pharynx, esophagus and colon. Emergence in use of small molecule and biologically-targeted agents for cancer have brought with them new GI toxicities with features of pathogenesis that are both overlapping and unique to the class. To date, the role of nutrition in cancer has been predominantly focused on supportive management of malnutrition, which is clearly associated with treatment response. GI toxicities including anorexia, nausea, diarrhea and constipation could all potentially be better managed with tailored nutritional therapy. New models have uncovered the mechanisms underpinning nutrient loss during cancer treatment and modeled ways to improve delivery, which will advance therapy options. As such, there are substantial opportunities to apply nutritional science to GI toxicity management in cancer therapy, which will be highlighted in this presentation.

## MOLECULAR MODULATION OF EDIBLE BIRD'S NEST EXTRACT ON CELLULAR REPAIR AND REGENERATION

***Chua Kien Hui***
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Edible bird's nest (EBN) has long been used by Chinese as traditional medicine since thousand years ago. Frequent consuming EBN is believed to enhance skin complexion, relieve asthma, strengthen immune system and retain youthfulness. Recent scientific data showed the functional compounds in EBN are glycoproteins or glycopeptides. For the past 15 years, various human cellular models had demonstrated the effects of EBN glycoproteins through molecular modulation. EBN glycoproteins are water-soluble and can be extracted with hot water. Direct exposure of EBN extract onto human fibroblast primary culture could evaluate its benefit to the human skin. Fibroblasts can be challenged with hydrogen peroxide as injury model or induce aging model to determine the effects of EBN extract by molecular modulation. For anti-osteoarthritis potential of EBN extract, human osteoarthritic chondrocytes were isolated from total knee replacement specimen and culture to determine the effects of EBN extract on cartilage degeneration problem. For cornea injury and parasite infection, the rabbit's corneal keratocytes and epithelial cells were cultured and challenged with acanthaemoeba to evaluate the potential of EBN extract for corneal wound repair. Lately EBN extract was identified to show mitogenic effect similar to epithelial growth factor, thus human adipose-derived stem cells culture were added with EBN extract and determine its proliferative effect and ability to maintain the stem cell multipotent potential. Besides, a cancer cell line, MCF7 was also used to evaluate the effects of EBN extract on anti-cancer potential and to understand its mechanism. There are different glycoproteins can be extracted from EBN, each has specific molecular weight and characteristics. More works need to be continue in order to understand the detail molecular interaction of EBN's glycoproteins on cellular signaling for health improvement and disease treatment.

# THEME II: UPDATES IN NUTRITION, HEALTH AND DISEASE

## OXIDATIVE STRESS AND THYROID DISORDERS

***Sarni Mat Junit***
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Thyroid gland is an endocrine organ that synthesizes thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Normal thyroid function is essential for development, growth, and metabolic homeostasis. The synthesis of thyroid hormones is under the influence of thyrotropin (TSH) and requires iodine and hydrogen peroxide ($H_2O_2$). Binding of TSH to TSH receptors on thyroid cells stimulates the synthesis of $H_2O_2$, which is the substrate of thyroperoxidase for thyroglobulin iodination during thyroid hormone synthesis. In thyroid follicles, $H_2O_2$ is generated at the apical membrane facing the follicular lumen as well as at the intracellular space by NADPH dual oxidases, DUOX2 and NOX4, respectively. Mutations in the gene encoding DUOX2 lead to congenital hypothyroidism due to insufficient $H_2O_2$ production. Similar to others, thyroid cells contain antioxidant enzymes to protect them from $H_2O_2$-mediated oxidative damage. Oxidative imbalance may result in thyroid cell dysfunction and thyroid diseases including cancers. Papillary thyroid carcinoma (PTC) is the most common thyroid cancer while medullary carcinoma is the rarest but most aggressive. There are growing evidence that benign thyroid lesions like multinodular goiter (MNG) can develop into PTC. Oxidative imbalance in the thyrocytes could trigger molecular changes including the somatic $BRAF^{V600E}$ mutation. PTC is usually a slow growing cancer with a low death rate. The presence of the $BRAF^{V600E}$ mutation is however, associated with a faster rate of growth and spread of the cancer and a higher risk of death. Serum protein profiles and gene expression patterns in PTC patients with MNG background differ from those without the MNG background suggestive of differences in the underlying molecular mechanisms.

## GENE POLYMORPHISM IN DIABETES MELLITUS AS RISK PREDICTION

***Rohana Abdul Ghani***
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Diabetes mellitus is a chronic condition characterised by a state of hyperglycaemia. The 2 main types of the illness share the same metabolic abnormality but have contradicting underlying pathophysiological processes; Type 1 (T1DM) being a state of insulin deficiency whilst Type 2 (T2DM) exist in a state of hyperinsulinaemia and resistance. The understanding of gene polymorphism in both types 1 and 2 diabetes mellitus has evolved over time. However, the practical value of identified genetic abnormalities in personalized risk prediction for the disease is still debatable, partly because the effect is relatively weak and adds little to predictions in comparison to other known conventional risk factors. In Type 1 diabetes mellitus (T1DM), there had been little genetic understanding because of limited number of samples available for analysis. However, the Type 1 Diabetes Genetic Consortium (T1DGC) has shed new light on T1DM due to the significant collection of renewable genetic materials for use in family based linkage and association studies which had provided deeper understanding of the associations between autoimmunity and genetic variants. Our local data reported the unique HLA-DR and DQ markers in the Malay population, with a risk prediction

model for type 1 DM in this population based on the quantitative presence or absence of a susceptible *HLA- DRB1*0301* allele and a protective *HLA-DQB1*0601* allele, respectively.
Type 2 diabetes mellitus (T2DM) has proven to be a bit more complex. Some authors suggested that the combined effect of a large number of genetic markers could have similar effect to that of some other recognised risk factors. However, large epidemiological data concluded that the genetic risk factors for T2DM may play a role in improving the predictive accuracy in addition to other anthropometric, biochemical, family history and other clinical risk factors.

## NUTRIGENOMICS AND EPIGENETICS IN OXIDATIVE STRESS FOR AGING WELL

***Der Jiun Ooi*** [1,2]*, *Maznah Ismail*[1], *Mustapha Umar Imam*[1], *Hadiza Adamu Altine*[1] *and Abubakar Bilyaminu*[1]
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Getting older is inevitable. The irreversible aging process (at least with the use of present technology), may however, be controlled or slowed down. From Aging to Aging Well, the underlying key may be the implications of epigenetics on the nutrigenomic responses to dietary factors in aging. The free radical and mitochondrial theories of aging proposed that age-associated accumulation of reactive oxygen species leads to a decline in cellular repair mechanisms. Oxidative damage causes a wide range of DNA lesions leading to mutations and further deranges the epigenetic state of the cell. Food choices and dietary intakes may alleviate or worsen the condition, depending upon the influences of nutrients and bioactives on gene responses in accordance with the underlying epigenetic traits. The research conducted by our group has shown that germinated brown rice (GBR), as a whole grain or in the form of extract/ rich fraction, mediate oxidative stress through improvement in antioxidant capacity, partly via transcriptional regulation of antioxidant genes. Surprisingly, the protective effects of GBR may also underlie epigenetics changes and transcriptional implications that led to improved metabolic outcomes in offspring of rats, following intrauterine exposure. It is postulated that bioactive compositions of maternal diets may directly or indirectly modulate the epigenetic machinery and nutrigenomics responses. The inheritable epigenetic traits could have transgenerational implications that might determine the different health outcomes well before the birth of an individual. Greater understandings into the epigenetic regulation of nutrigenomic responses may provide more insights on how the Aging Well concept can be optimized to improve the quality of life, health, and longevity.

## CHEMOPREVENTIVE PROPERTIES OF PHYTOCHEMICALS: MOLECULAR INSIGHT

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Current research in drug discovery, pharmacology and molecular biology has emerged the term chemoprevention or prevention of cancer. It is defined as the use of natural or synthetic subtances in preventing or suppressing the cancer formation or cancer progress. Two main categories of chemopreventive agents are blocking and suppressing agents. For instance, blocking agents prevent carcinogens from reaching the target sites from undergoing metabolic activation or subsequently interacting with crucial cellular macromolecules such as deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and proteins. Meanwhile, suppressing agents inhibit the malignant transformation of initiated cells either the promotion or progression stage. Remarkable progress in cellular and molecular biology over the past decades led to a deep insight into the biochemical events associated with the multistage process of carcinogenesis. Evidence that phytochemicals (non-nutritive components in the plant-based diet) possess substantial chemopreventive properties is increasingly being reported in the scientific literature. Hence, it is important to identify molecular targets that are associated with each stage in the natural history cancer and are modulated by chemopreventive phytochemicals. One of the example is curcumin from *Curcuma longa* L. which inhibits chemically induced carcinogenesis during initiation, promotion and progression of colon cancer. Other examples of phytochemicals include resveratrol, proanthocyanidin, lycopene, sulforaphane, gingerol and genistein. Hence, the quest of novel phytochemicals from various plants such as *Annona muricata* (soursop), *Hedyotis corymbosa* (pearl grass), *Cosmos caudatus* (Kenikir) and *Pilea trinervia* (Pohpohan) as chemopreventive agents is greatly needed which can be beneficial for the prevention of cancer.

## INTESTINAL BARRIER IN HEALTH AND DISEASE: POSSIBLE ROLE OF NUTRIENTS

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In addition to digestion and absorption of food, intestinal mucosa acts as a barrier known as intestinal barrier (IB) between the lumen of the intestine and internal organs of the body. A healthy IB prevents the passage of harmful antigenic materials from the intestinal lumen into the systemic circulation. A compromised IB increases intestinal permeability which has been considered to be the primary event in the pathogenesis of several diseases. Until now, no medicines are available to strengthen IB but several nutrients have been reported for their beneficial effects on the IB. Objective of this talk is to provide an overall idea of IB in health, causes and underlying pathophysiology of compromised IB in various physiological and pathological conditions and the nutrients to ameliorate such changes. In healthy individuals, IB is formed and strengthened mainly by the mucus layer, enterocytes, tight junction proteins etc. and prevents excessive passage of harmful materials from the lumen. Disruption of IB occurs with ageing, unhealthy eating habit especially consumption of high calorie and high fat diet, in inflammatory bowel disease, autoimmune diseases etc. Several nutrients such as zinc, glutamine, vitamin A and few more have the potential to ameliorate the changes of IB in various conditions. Intake of appropriate nutrients might restore IB and prevent different diseases related to compromised IB.

# FREE COMMUNICATIONS

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**FREE ORAL COMMUNICATION**

**POSTER PRESENTATIONS**

## FREE ORAL COMMUNICATIONS

### O-1

### Tocotrienol Administration Restores Estrogen and Progesterone Receptor Expression in Ovaries of Cyclophosphamide Treated Mice: An Implication for Ovary Protection in Chemotherapy

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**Introduction:** Cyclophosphamide (CPA) chemotherapy causes infertility via oxidative stress-induced apoptosis of ovarian cells, leading to ovarian failure. Tocotrienol (T3) is a potent antioxidant and anti-inflammatory agent. The role of T3 in ovarian protection throughout chemotherapy remains un-elucidated. Aim: To determine ER and PR gene expression and evaluate localization expression of ER and PR expression in ovarian cells with CPA and concurrent treatment of CPA and T3. **Methods:** Sixty female ICR mice, aged 8 to 10 weeks were divided into 5 treatment groups: CPA, CPA&T3, normal saline, T3 only and corn oil only. The treatment was given for 30 days, followed by administration of pregnant mare serum gonadotrophin and human chorionic gonadotrophin to induce super ovulation. The mice were euthanized at 14 to 16 hours post induction and the ovaries were dissected; one was fixed in 10% formalin, processed and embedded in paraffin to form tissue blocks. The other ovary was immediately preserved in liquid nitrogen for RNA extraction and cDNA synthesis with real-time quantitative PCR. Concentration of the forward, reverse primers, probes, cDNA template, as well as the annealing temperature were optimized using ER, PR, GAPDH and β-actin genes. All IHC reactions were performed using a kit and monoclonal mouse primary antibody. All data were subjected to statistical analysis by one-way ANOVA and Repeated Measure ANOVA. **Results:** CPA treatment caused ER and PR gene expression to increase above normal. Co-administration of CPA&T3 significantly decreased the expression these genes. Immunohistochemistry showed derangement of ER and PR expression patterns with CPA administration. The ER and PR expression was restored to near normal in CPA&T3 group ($p<0.05$). **Conclusion:** Co-administration of T3 with CPA led to restoration of balanced ER and PR expression in ovaries of CPA treated mice. T3 is a potential candidate for ovarian preservation in chemotherapy-associated damage.

### O-2

### Expression of Anti-Apoptotic Factor In Oocytes from Aging Mice Supplemented with Tocotrienol-Rich Fraction

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**Introduction:** Ovarian aging is accompanied by a decrease in quantity and quality of oocytes which profoundly affects fertilization and subsequently embryonic development. Oxidative stress is one of the key factors that induce oocyte apoptosis in aging. Tocotrienol-rich fraction (TRF), a potent antioxidant, has been proven to exert protective effects on female reproductive system. Thus, this study was performed to determine the effect of daily supplementation of TRF on the quality of oocyte and its mechanism of action in aging mice. **Methods:** Female *Mus musculus* mice were divided into four groups. Six-month-old mice were given tocopherol-stripped corn oil as a vehicle control while other groups were supplemented orally with TRF at doses of 90, 120, and 150 mg/kg body weight for two months, respectively. After two months, mice from all groups were superovulated and euthanized. Oocytes were collected and examined for its morphology. The estimation of pro/anti-apoptotic factors in oocyte was done using enzyme-linked immunosorbent assay (ELISA) kit. **Results:** The percentage of normal oocytes were significantly higher ($p<0.001$) and the fragmented oocytes were significantly lower ($p<0.001$) in TRF supplemented group. The expression of Bax (pro-apoptotic factor) was significantly higher ($p<0.001$) in aging group. In contrast, the expression of Bcl-2 (anti-apoptotic factor) was significantly higher ($p<0.001$) in TRF supplemented group. The Bax/Bcl-2 ratio was significantly higher in aging group and significantly lower in TRF supplemented group. This implies that modulation of Bax to Bcl-2 could be used to determine the quality of oocytes. **Conclusion:** It is suggested that TRF supplementation improves the quality of oocytes derived from aging mice and the proposed mechanism of action is by reversing the expression of apoptotic factors.

## O-3

## Elucidating the Functions of FBXW7 R479Q in Colorectal Cancer

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**Introduction:** FBXW7 is a tumour suppressor gene and is mutated in ~14% colorectal cancer (CRC). Our whole genome sequencing (WGS) in CRC patients identified missense alteration in exon 10 of the gene which denoted as R479Q. *FBXW7* is involved in ubiquitin mediated proteolysis, a process which lead to protein degradation by the ubiquitin-proteasome system. This gene regulates various oncogenic proteins, hence the loss of *FBXW7* may result in failed regulation and accumulation of its downstream proteins targets, leading to oncogenesis and progression of multiple cancers including CRC. *FBXW7* loss is associated with chemoresistance to 5-fluorouracil; however, the consequences and functions of *FBXW7* R479Q has not been extensively elucidated. This study aims to investigate the role of *FBXW7* R479Q in CRC carcinogenesis and its involvement in ubiquitin-mediated proteolysis. **Methods:** Sanger sequencing was performed to validate the mutation identified via WGS. Site directed mutagenesis was performed to introduce *FBXW7* R479Q in a wild type *FBXW7* plasmid. The mutant (*FBXW7* R479Q) plasmid and *FBXW7* wild type were transfected into HEK-293T cell lines. Protein was extracted from the transfected cells and the effect of the mutation of protein ubiquitination was assessed using Proteome Profiler Human Ubiquitin Array. Quantitative polymerase chain reaction

(qPCR) was performed to assess *FBXW7* gene expression. Western blot was performed to assess the c-Myc protein expression. Student's T-test was performed using GraphPad Prism and p value < 0.05 was considered as significant. **Results:** *FBXW7* R479Q led to reduced expression. Thirty-eight proteins showed significantly reduced ubiquitination levels in FBXW7 R479Q mutated cells compared to the wildtype. **Conclusion:** *FBXW7* R479Q may play an important role in the pathogenesis of CRC via ubiquitin-mediated proteolysis.

**O-4**

## The Effect of Integrin N-Glycan Processing Inhibition in The Migration of Osteosarcoma Cell Line

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**Introduction:** Integrin, a cell surface adhesion receptor for the extracellular matrix proteins, plays a crucial role in tumor metastasis. Binding of integrin with its ligand, activates intracellular signaling cascades that lead to malignant transformation of cells. Aberrant glycosylation of integrin has been observed in many cancers including osteosarcoma (OS). However, the effect of alteration in integrin glycosylation process, mainly during *N*-glycan processing in the OS cell line has yet to be elucidated. Therefore, the objective of this study was to investigate the effect of integrin glycosylation inhibition towards OS metastasis. **Methods:** In this study, alterations of integrin glycosylation process were carried out by treatment of OS cell line (MG-63) with deoxynojirimycin (DNJ); an inhibitor for α-glucosidase-I and II (0.25, 0.5, 1.0, 2.0, and 3.0 mM) and deoxymannojirimycin (DMJ); an inhibitor for α-1-2 mannosidase (0.25, 0.5, 1.0, 2.0, and 3.0 mM) respectively at 6, 12, 18, 24, and 48-hour time points. Then, cell viability and migration capacity of the cells were determined using MTS and cell invasion assay, respectively. **Results:** Neither DNJ nor DMJ (0.25, 0.5, and 1.0 mM) had any effect on the cells viability at any time point. However, both DNJ and DMJ at 2.0 and 3.0 mM decreased cell viability to less than 50%. Treatment of MG-63 cells with 1.0mM DNJ showed significant increase in cell migration capacities. On the other hand, treatment of MG-63 cell line with 0.5 mM DMJ significantly decreased cell migration capacity. **Conclusion:** Based on the results obtained, it is proposed that the interference of α-1-2 mannosidase activity in the integrin glycosylation process of OS cell lines did not show reducing effect on its invasion rate through the extracellular matrix layer. However, targeting α-glucosidase-I and II activity may help in the down regulation of OS cancer progression.

**O-5**

## Consumption of Polyphenols-rich Tropical Fruit Juice Showed to be Beneficial towards Cognitive Status, Oxidative Stress and Metabolomic Profiles among Middle-Aged Women

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**Introduction:** Age-related cognitive decline starts to show its sign during middle-age and is greatly affected by dietary factors. Polyphenols have received attention in its role to improve health issues related to aging, including decline in cognitive status. Therefore, the study aimed to determine the effects of polyphenols-rich tropical fruit TP 3-in-1™ juice in improving cognitive status, oxidative stress and metabolomics profiles among middle-aged women. **Methods:** This study involved a clinical trial among middle-aged women (aged 50.8 ±3.7 years) with signs of poor cognitive status as assessed using Rey's Auditory Verbal Learning Test (RAVLT), who were randomised to receive supplementation of TP 3-in-1™ juice (n=16) or placebo (n=15). Supplementation was given for three days in a week for a period of ten weeks. Outcome measures were changes of cognitive status, concentration of malondiadehyde (MDA) and metabolite profiles throughout the intervention. **Results:** There was significant interaction effects on RAVLT immediate recall ($p<0.05$) and Comprehensive Trail Making Test (CTMT) Trail 4 ($p<0.05$). For oxidative stress, there was a significant time effect ($\eta p^2=0.17$; power=0.63, $p<0.05$). Metabolomics analysis showed the presence of metabolites related to polyphenols intake and cognitive functions with the intervention group showed increased urinary excretion of thyroxine and 3-methyladenine. Thyroxine and 3-methyladenine provide stability to human transthyretin (TTR) and activates autophagy, respectively, which were associated with Alzheimer's disease. **Conclusion:** Early detection of poor cognitive status is crucial among the middle-aged adults, which may lead to Alzheimer's disease in old age. Supplementation of TP 3-in-1™ juice for 10 weeks has the potential to improve cognitive status related to learning, memory and processing speed among middle-aged women due to its anthocyanins content. Metabolomics result showed increase in the urinary concentration of thyroxine and 3-methyladenine, which provide stability to human TTR and activates autophagy, respectively, which is associated with Alzheimer's disease.

## O-6

## Effects of Integrin Glycosylation Inhibition on Extracellular Matrix (ECM) Adhesion Proteins in Osteosarcoma Cell Lines MG63

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**Introduction:** Integrins are cell surface membrane receptors that mediate cell-cell and cell-extracellular matrix (ECM) interactions. It has been well established that glycosylated integrin plays a role in cancer progression, particularly the adhesion, migration and invasion. We hypothesised that in osteosarcoma (OS), its invasive capacity can be reduced by inhibiting glycosylation of the integrins via the ECM proteins. Therefore, this study aims to investigate the effects of integrin glycosylation inhibition on the ECM proteins. **Methods:** Deoxynoririmycin (DNJ) was used to inhibit the integrin glycosylation in MG63 cells. The cells were seeded in a 96-well plate and treated with 0.5mM DNJ for 24 hours. The cell adhesion assay was performed using ECM cell adhesion array kit. **Results:** Among the seven ECM proteins tested, it was found that collagen type II and IV, fibronectin, laminin and tenascin showed decreased cell adhesion compared to non-treated MG63 cells. Meanwhile, collagen type I and vitronectin showed an increase in cell adhesion compared to non-treated cells. Previous studies have reported that collagen, fibronectin and laminin have enhanced migration and invasion in tumour cells, which is in accordance to our results. As the ECM proteins served as molecular scaffold for cell adhesion and migration as well as ligands for the integrins, inhibition of integrin glycosylation could affect the binding of the ECM proteins, as shown in the decreased cell adhesion activity. However certain ECM proteins could be affected differently as shown by collagen type I and vitronectin, which deemed further investigation. **Conclusion:** The results showed prominent changes in the cell adhesion rate of the ECM proteins towards integrin upon glycosylation inhibition. This could be attributable to changes of the integrin binding site due to the glycosylation inhibition, which in turn reduced or increased the adhesion rate of the ECM proteins.

## O-7

## Changes in Metabolomics Profile At Different Stages of Colorectal Cancer

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**Introduction:** Colorectal cancer (CRC) is one of the leading causes of cancer related death in the world. Early diagnosis and accurate staging of this cancer is vital to improve prognosis. However, the molecular changes involved in the progression of this cancer are not clear. In this study, global metabolomics profiling was performed by using CRC cells of different stages (Duke's A, B, C and D) in order to identify differentiating metabolites as well as unravel the pathophysiology involved in its progression. **Methods:** Metabolomics profiling from intracellular was analyzed by LC/MS QTOF 6250 Agilent and metabolites were determined using METLIN database. **Results:** There are 26 metabolites which were significantly different in different stages of CRC. These metabolites include (Z)-13-Oxo-9-octadecenoic acid, 1,2,4-Nonadecanetriol, 2-Methylbutyroylcarnitine, acetylcarnitine, armillaripin, flavin adenine dinucleotide (FAD), flavine mononucleotide (FMN), glucose 6-phosphate, hexadecanoic acid, L-lactic acid, L-Leucine, L-Methionine, L-Phenylalanine, L-Tryptophan,lumichrome,lysoPE(0:0/16:0),lysoPE(0:0/16:1(9Z)),lysoPE(0:0/20:4(5Z,8Z,11Z,14Z)),lysoPE(0:0/20:5(5Z,8Z,11Z,14Z,17Z)),lysoPE(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0),N,N'-Bis(gamma-glutamyl) cystine, pantothenic acid, phytosphingosine, pipericine, riboflavin, and tetradecanoylcarnitine. By using Metaboanalyst 3.5, PLS-DA scores plot able to discriminating the CRC cell from different stages, while L-methionine showed the highest VIP scores identified by PLS-DA. The pathway analysis showed metabolism of riboflavin is the most pertubated. **Conclusion:** Deficiency of methionine and riboflavin may influence carcinogenesis due to their roles in the one-carbon metabolism pathway which is critical for DNA synthesis, methylation and repair. This study highlights the metabolite changes and the pathway affected from different stages of CRC cell and the potential biomarkers that can be used for staging of CRC.

**O-8**

## Contrariwise Effect of Oxidised High Density Lipoprotein in Inducing Vascular Calcification and Osteoblast Decalcification

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**Introduction:** Vascular calcification and osteoblast decalcification have been suspected as the main factors to induce the development of atherosclerosis and osteoporosis respectively. Lipid peroxidation is one of the modifications that occur to HDL which alter its physiological roles and was postulated to be linked with the afore mentioned two conditions. However, the connection is still not clear. **Methods:** Cytotoxicity effect of oxHDL (10, 25, 50, 100 µg/ml) in both human vascular smooth muscle cells (HVSMC) and human osteoblast (NHOst) were measured by CellTiter 96® AQueous One Solution Cell Proliferation Assay. Oxidized HDL (oxHDL) at 10, 25, 50, 100 µg/ml was incubated with HVSMC and NHOST respectively for 14 days and were stained with 2% alizarin red for detection of mineral nodules. Calcium deposition inside the cells were analyzed by calcium colorimetric assay. **Results:** Cytotoxicity results showed that oxidized HDL at 10, 25, 50, 100 µg/ml was not toxic to both cell types. oxHDL induced formation of mineral nodules and depositing of calcium in

HVSMCs in a dose dependent manner compared to negative controls ($p<0.05$) where 100 µg/mL showed the highest induction. On the other hand, oxHDL reduced the formation of mineral nodules and production of calcium in NHOst compared to negative controls ($p<0.05$). Oxidized HDL at 50 µg/mL showed the highest inhibition of mineralization in NHOst. **Conclusions:** This study shows the ability of oxHDL to induce vascular calcification and bone demineralization. This suggests a dual but opposing effect of oxHDL on vascular smooth muscle and osteoblast cells. We suggest that oxHDL is the link between osteoporosis and vascular stiffness among patients with atherosclerosis.

**O-9**

## Evaluate the Effect of Filtrates of Fungi Contaminating Wheat Grains on Wheat Grains Germination and Study the Effect of Acetonic Extract of *Capsicum Onnuum* on the Growth of the Isolated Fungi

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**Introduction:** Wheat is one of the world's largest and most essential food crops. It covers a significant portion of the earth's surface, greater than any other plant. It tends to be among the top strategic crops. Wheat contamination with *Aspergillus* leads to rapid deterioration of quality and quantity of wheat products. Wheat grains are exposed to various fungi during its growth stages and storage. Many of those molds are potential mycotoxins producers that will produce different harmful consequences for the yield quality as well as population health. The present work aimed to isolate and identify the fungi which contaminate the wheat grain from the Misurata Agricultural Research Center area and South Region of Libya. **Methods:** Fungi contaminated wheat grains were isolated on Sabouraud Dextrose Agar and identified by culture and microscopic observation. Fungal filtrates of two fungal isolates, *Aspergillus Niger*, and *Rhizopus sp*, were investigated for their effects on the germination and seedlings of wheat grains. Furthermore, the effect of acetone extracts of chili pepper (*Capsicum onnuum*) on the vegetative growth of isolated fungi was also investigated. **Results:** Ten types of fungi belonging to four genera were isolated and identified. The germination rate of wheat grains irrigated with the filtrate of *A. Niger* and *Rhizopus sp* was 20% and 80% respectively compared to 98% of the control grains which were irrigated with potato dextrose broth. The acetone extract of *Capsicum onnuum* showed a disincentive effect (85%) on the germination of the fungal spore contaminated wheat grains. **Conclusion:** This study concludes that the fungal secretions have pathogenic effects on plant growth which can also cause health problems for the human population. Biological control such as plant extracts can be an alternative to chemical pesticides to control pathogens and their secretions.

## O-10

## Serum Acetylcarnitine and Hypoxanthine as Biomarkers for Colorectal Cancer

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**Introduction:** Currently, the diagnostic tools for colorectal cancer (CRC) involves invasive techniques such as colonoscopy and histopathology. Other screening tests are neither accurate nor specific. This contributes to the late diagnosis of CRC. For better prognosis, a more accurate, specific and non-invasive test is needed. **Methods:** Serum samples from 50 healthy controls and 50 colorectal cancer patients were collected at Hospital UKM. The samples were deproteinised with acetonitrile and the metabolomics profile determined using liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOFMS, Agilent USA). The data were analysed using Mass Profiler Professional (Agilent, USA) software. **Results:** The levels of acetylcarnitine and hypoxanthine were significantly different between CRC and normal controls. The altered levels of these metabolites were presented in 80% of CRC patients. Based on analysis of area under the curves, these metabolites showed high sensitivity and specificity as biomarkers. The alterations in these metabolites revealed perturbations in purine metabolism and fatty acid oxidation. **Conclusion:** The results suggest the potential of measuring serum acetylcarnitine and hypoxanthine levels as biomarkers for CRC.

## O-11

## Effect of Phoenix Dactylifera and Goat Milk on Iron Deficiency Anaemia in Rats

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**Introduction:** Iron deficiency anaemia (IDA) is the most common micronutrient deficiency in the world characterised by poor haemoglobin (Hb) content and poor iron store. It is common in underprivileged areas and indicates poor nutrition and health. According to Islamic belief, dates and goat milk are considered as super foods for health. Therefore, this study aimed to determine the beneficial effects of dates and goat milk on haematological parameters, iron store and the iron bioavailability in IDA animal model. **Methods:** IDA model Wistar rats were used in the study. They were randomly divided into groups with different feeding protocol (dates, goat milk, dates and goat milk, ferrous fumarate) for 4 weeks. Full blood count and iron profile were assessed at the beginning of the study and repeated at week 4. Iron bioavailability was assessed by haemoglobin regeneration efficiency (HRE). Data were analysed by one-way analysis of variance ANOVA using SPSS 23.0 software with p value $< 0.05$ considered as statistically significant. **Results:** There was significant improvement in haemoglobin (Hb) concentration, red blood cell (RBC) count, packed cell volume

(PCV) and serum iron level in all treatment groups ($p < 0.05$). The haemoglobin regeneration efficiency (HRE) was significantly improved in all treatment groups when compared to IDA control group ($p < 0.05$). **Conclusion:** The present study revealed that dates and goat milk improve the haematopoietic parameters, iron profile and HRE in IDA rat model. This may be contributed by the high iron content in dates and presence of biochemical components in dates and goat milk that enhanced iron bioavailability. Therefore, inclusion of dates and goat milk may be considered as a supplementary diet in IDA subjects as well as prevention in context of balanced diet for those at risk of IDA.

**O-12**

## Energy-Metabolism Related Gene Expression in Iron Deficiency Anaemia Treated with *Phoenix Dactylifera* and Goat Milk

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**Introduction:** Iron deficiency anaemia (IDA) is a global problem related to malnutrition. It causes fatigue and impairs mental development in children. Dates and goat milk are mentioned in the Quran and Sunnah as superfoods and many scientific studies reported that dates and goat milk can improve energy metabolism in IDA. Hence, this study aimed to evaluate the effects of dates and goat milk on expression of energy metabolism-related-gene in iron deficient rats. **Methods:** IDA model Wistar rats were divided randomly and received different type of treatments; dates, goat milk, both dates and goat milk and ferrous fumarate for 4 weeks. Tissues from liver and muscle were harvested for quantitative real-time PCR of energy metabolism-related genes expression level. The genes of interest were PFKL, G6PC, ALDOB, MT-ATP6 and MT-CYB which are involved in cellular energy metabolism pathways specifically glycolysis, gluconeogenesis and electron transport chain (ETC). Results were analysed using one-way analysis of variance (ANOVA) test by SPSS 23.0 software with p value $< 0.05$ considered as statistically significant. **Results:** There was a significant increase of the genes MT-CYB ($p<0.01$) and MT-ATP6 ($p<0.05$) expression in the group treated with both dates and goat milk compared to IDA control group. No significant difference was observed in PFKL expression, while for G6PC and ALDOB, the significant increase in treated group was observed only when compared to normal control. **Conclusion:** Inclusion of dates and goat milk in IDA model's diet results in over expression of energy metabolism-related-genes specifically in the ETC pathway which is the main ATP producer. This may be due to the high iron content in dates and phosphorus in goat milk that could compensate the generation of ATP via formation of NADH which needs iron as the cofactor. Increased in the production of ATP improve energy metabolism of IDA subjects.

## POSTER PRESENTATIONS

### P-1

### Alpha Tocopherol Improves Mitochondrial Ultrastructure and Preimplantation Development of Murine Embryos

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**Introduction:** Alpha-tocopherol is an antioxidant that can improve reproduction. Studies have shown that α-tocopherol added to culture media improves mitochondrial activity, gene expression and development in embryos. However, there are no reports on the effect of α-tocopherol maternal supplementation on mitochondrial ultrastructure and embryonic development. Aim of this study was to investigate the effects of maternal supplementation of α-tocopherol on mitochondrial ultrastructure and preimplantation development. **Methods:** Female C57Bl/6 mice were supplemented with 60 mg/kg body weight per day of corn oil stripped of α-tocopherol (control) or α-tocopherol (treatment) for seven days. They were superovulated and mated with fertile males to obtain 2-cell stage embryos. Normal 2-cell embryos were observed in culture until the blastocyst stage. At the 8-cell stage, embryos were subjected to transmission electron microscopy (TEM) to observe their mitochondria. The embryos were fixed with glutaraldehyde and osmium tetroxide before serial dehydration with acetone and resin infiltration. They were subjected to ultramicrotomy before lead citrate and uranyl acetate staining. **Results:** In culture, α-tocopherol produced significantly higher numbers of 4-cell stage and blastocysts, compared to controls [(96.6% vs 89.2%) and (66.9% vs 52.2%), $p < 0.01$]. In comparison to control, the α-tocopherol treatment group embryos had more mitochondria, with distinct cristae. **Conclusion:** Alpha-tocopherol maternal supplementation improved mitochondrial ultrastructure and preimplantation development of murine embryos.

### P-2

### Physicochemical Properties and Sensory Analysis of Breakfast Cereal Added with Tiger Milk Mushroom (*Lignosus Rhinocerus*) Sclerotium Powder

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**Introduction:** Current studies for tiger milk mushroom only available in pharmaceutical field. Thus, there are some researchers that encourage consumers to

use this Tiger milk mushroom sclerotium powder to be added in the food as it is to imitate indigenous people for their health benefits in foods and acts as decoction. The objective of this study is to determine the composition of the Tiger milk mushroom (*Lignosus rhinoceros*) (TMM) sclerotium powder that has been added into the breakfast cereal that acts them as functional food ingredients. **Methods:** The formulations for breakfast cereal added with Tiger milk mushroom sclerotium powder have five formulations that have been examined which are Control (0% of TMM sclerotium powder), F1 (0.05% of TMM sclerotium powder), F2 (0.10% of TMM sclerotium powder), F3 (0.15% of TMM sclerotium powder) and F4 (0.20% of TMM sclerotium powder). Physicochemical properties were analysed for these cereals. **Results:** There are no significance difference in proximate analysis, physical attributes and sensory analysis among formulations. Total phenolic content and DPPH radical scavenging exhibited increasing antioxidant activity when greater ratio of Tiger milk mushroom sclerotium powder added in breakfast cereal. **Conclusion:** All of the formulations were acceptable as the TMM sclerotium powder does not affects the taste and attributes of the breakfast cereal. Formulation 4 (0.20% TMM powder) indicated higher total phenolic content (0.70 mg/GAE g) compared to Formulation 1 (0.32 mg/GAE g). Similarly, higher DPPH radical scavenging activity was found in Formulation 4 (88.03%) compared to formulation 1 (82.63%).

**P-3**

## The Expression of DNA Damage Response Genes in Mice Ovary Exposed to Corticosterone-Induced Oxidative Damage: Role of Tocotrienol-Rich Fraction Supplementation

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**Introduction:** Chronic exposure to corticosterone (CORT) induces oxidative stress that may lead to DNA damage in cells and in female reproductive system it will negatively influence reproductive outcome. Tocotrienol-rich fraction (TRF) was reported to play protective role in oxidative stress-induced DNA damage thus prevent infertility in female. We investigated the expression of DNA damage response genes which play significant role in activating various signalling network to detect and repair the oxidative stress induced-DNA damage in mice ovary exposed to exogenous CORT. **Methods:** Six-week-old female mice (Mus musculus) were administered i) vehicle control via intraperitoneal (i.p.) injection ii) CORT 10 mg/kg body weight (BW), iii) vehicle control via i.p injection and oral gavage iv) CORT (10 mg/kg BW, i.p injection) and concurrently supplemented with TRF (150 mg/kg BW, oral gavage) for two weeks. At the end of supplementation period, mice were euthanized and the ovaries were collected for total cellular RNA isolation. The gene expression analysis of ATM, MPG, CHEK1, CHEK2 and MLH3 genes was performed using QuantiGene Plex 2.0 Assay kit and all data obtained were analysed with one-way ANOVA. **Results:** The expression of CHEK1 was significantly higher ($p<0.05$) in the mice exposed to exogenous CORT as compared to the control group. The expression level of CHEK1

gene in CORT group supplemented with TRF on the other hand was found to be normalized towards its control value. However, expression of other DNA damage response genes was not significantly different as compared to their respective controls. **Conclusion:** It is suggested that the role of TRF as an antioxidant is by blocking the adverse effect of exogenous CORT in inducing oxidative stress DNA damage in mice ovary. This was indicated by the low expression of CHEK1 gene that detects DNA damage in ovary following TRF supplementation in mice exposed to exogenous CORT.

**P-4**

## Vitrification of Murine Embryos from Females Supplemented with Palm Tocotrienol-Rich-Fraction

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**Introduction:** In Assisted Reproductive Technology (ART), cryopreservation is essential for the storage of embryos. Palm tocotrienol-rich fraction (TRF) contains both tocopherols and tocotrienols. These isomers of Vitamin E have been reported to improve preimplantation development of embryos. However, there are no reports on the use of palm TRF to improve embryonic vitrification outcomes. The aim of this study is to determine the effect of vitrification on murine embryos from females supplemented with palm TRF, with emphasis on mitochondrial ultrastructure and preimplantation development. **Methods:** The C57Bl/6 females were given oral gavage of 60 mg/kg body weight per day of corn oil stripped of alpha-tocopherol (control) or TRF (treatment), for seven days. They were superovulated, mated and euthanized to acquire 2-cell stage embryos. For vitrification, normal 2-cell embryos were equilibrated with EFS20 and vitrified with EFS40 before immersion into liquid nitrogen. After sequential warming, the 2-cell embryos were cultured to the blastocyst stage. For TEM, blastocysts were fixed with glutaraldehyde and osmium tetroxide before serial dehydration with acetone and resin infiltration. They were subjected to ultramicrotomy before staining with lead citrate and uranyl acetate. **Results:** There were no significant differences in developmental competence between control and vitrified group embryos. In TRF group, the mitochondria were clustered around cryo-damaged organelles. **Conclusion:** Palm TRF maternal supplementation contributed to the recovery of vitrified embryos.

**P-5**

## The Effects of *Pandanus Amaryllifolius* Roxb. (PA) Leaf Water Extraction on Hypertension in Fructose Induced Metabolic Syndrome Rat Model

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**Introduction:** Metabolic syndrome which encompasses obesity, hypertension, hyperglycemia and dyslipidemia is increasing worldwide. Thus, preventive measures for this condition is very important. The usage of local Malaysians plant known as *Pandanus amaryllifolius* may have a potential effect to reverse hypertension. *Pandanus amaryllifolius* or also known as Pandan leaves contains flavonoids and phenolic acids as predominant phytochemicals. Therefore, the present study was conducted to investigate the effects of PA leaf water extract (PA) on hypertension in an established fructose-induced metabolic syndrome model in male Wistar rats. **Methods:** Thirty five, Wistar rats weighing between 150 to 200g were randomly divided into three groups: control (C), 10% PA leaf water extract (PA) and metabolic syndrome group (MetS). Food and fluid were given as ad libitum for eight weeks. These three groups received fluid which include tap water, 10% PA leaf water extract and 20% fructose drinking water in group C, PA and MetS respectively. After eight weeks, the MetS group were further subdivided into three subgroups namely MetS1, MetS2 and MetS3. MetS1 group was sacrificed as to be the control for the metabolic syndrome. MetS2 and MetS3 groups were treated with tap water and 10% PA leaf water extract respectively for another eight weeks. Blood pressure was measured using tail-cuff method at the baseline and at the end of the experiment. All data were presented in mean ± SEM subjected to one way ANOVA. **Results:** Treatment with10% PA leaf water extract in metabolic syndrome normalized the blood pressure in metabolic syndrome rats. **Conclusion:** These results showed that 10% PA leaf water extract helped to improve hypertension in metabolic syndrome rat model induced by fructose drinking water. We hypothesized that flavonoids and phenolic acid contained in PA may play an important role in this condition.

**P-6**

## *Pandanus Amaryllifolius* Roxb. (PA) Leaf Extract Attenuates Obesity in Fructose Induced Metabolic Syndrome Rat Model

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**Introduction:** Flavonoids and phenolic acids are predominant phytochemicals and antioxidant present in *Pandanus amaryllifolius* (PA) which could be beneficial to prevent an increasing common health problems which include obesity. This study was done to investigate the effects of PA leaf water extract in fructose induced metabolic syndrome rat model. **Methods:** Thirty Wistar rats weighing between 150 to 200g were randomly divided into three groups; control (C), 10% of PA leaf water extract (P) and metabolic syndrome (MetS). Food and fluid were given as *ad libitum* for eight weeks. These three groups were provided different types of fluid which include tap water, 10% PA leaf water extract and 20% fructose water in group C, PA and MetS respectively. After eight weeks, the MetS group were further subdivided into three group namely MetS1, MetS2 and MetS3. MetS1 group was sacrificed as to be the control for metabolic syndrome. MetS2 and MetS3 groups were treated with tap water and 10% PA leaf water extract respectively for another eight weeks. Parameters for obesity which include percentage of total body weight gain, body mass index, abdominal circumference (AC) and histomorphometry of abdominal adipose tissue were measured and analyzed. All data was presented in mean ± SEM subjected to one way ANOVA. **Results:** PA leaf water extract treatment significantly reduced the percentage of total weight gain and body mass index. However, it showed no changes in AC. Histomorphometry showed decreased in the size of adipocytes but was not statistically significant. **Conclusion:** These results showed that 10 % PA leaf water extract help to attenuate some of the parameter in obesity in fructose induced metabolic syndrome rat model. We hypothesized that prolongation of the duration of treatment could help to revert all parameters in obesity.

**P-7**

## The Effect of Honey as Supplementary Food on Glycaemic Control and Metabolic Parameters in Patients with Impaired Fasting Glucose

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**Introduction:** Impaired fasting glucose (IFG) increases the risk of cardiovascular disease. Honey can reduce hyperglycemia and ameliorate metabolic abnormalities Therefore some patients resort to consume honey.This study was aimed at determining the effect of honey as supplementary food on glycaemic control and metabolic parameters in IFG patients. **Methods:** This was a quasi-experimental study of 4 weeks duration. Inclusion criteria were adult patients diagnosed of IFG. Those currently taking herbal extract, history of drug or alcohol abuse and allergic to honey were excluded. Subjects were randomly allocated to either the experimental group (n = 30) or a control group (n = 30). The former received 30 g/day of kelulut honey. While the later did not receive honey. No advice given for special diet and exercise regimen. Anthropometric parameters, waist circumference, fasting blood glucose (FBG) and fasting lipid profile(FLP) were determined at day 1 and 4 weeks of intervention. Statistical analysis was undertaken with Graphpad Prism version 7 and a p value <

0.05 is considered statistically significant. **Results:** There were no significant difference of any variables at the end of 4 weeks in honey and non-honey supplementation group compared at day 1. However, there was a significant different of systolic blood pressure at the end of 4 weeks in non-honey supplementation group. None of the variables neither at baseline nor at 4 weeks of experiment between the groups showed statistically significant difference. However, there was a significant increase of total cholesterol level in honey supplementation group compared to non-honey at the end of the study. **Conclusion:** This study demonstrated that 4-week consumption of honey did not cause significant differences in FBS and other measured metabolic parameters. Hence it would be safe to consume honey by IFG as supplementation. Nevertheless further study is warranted to confirm the effect of honey on increasing blood cholesterol level.

**P-8**

## The Effects of Compound SNA209 on Angiotensin II-Induced Cardiac Hypertrophy in H9C2 Cardiomyocytes

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**Introduction:** Heart failure is one of cardiovascular diseases that increase mortality and morbidity rate globally. It is characterised by cardiac cell enlargement, known as cardiac hypertrophy, which can be induced by angiotensin II (Ang-II) in vitro. One pharmacological management for the heart failure is cardiac glycosides. Compound SNA209, isolated from *Cerbera odollam* leaves is structurally similar to the cardiac glycosides. Therefore, this study aimed to determine the effects of compound SNA209 on Ang II-induced cardiac hypertrophy in H9c2 cardiomyocytes. **Methods:** H9c2 cardiomyocytes were exposed to Ang-II (500 nM) in the absence or presence of the compound SNA209 (3 µM) or digoxin (5 µM) for 24 hours. Digoxin served as the positive control, while a group without any treatment was the negative control. SNA209 and digoxin were preincubated in the cells an hour prior to exposure to Ang II. **Results:** Ang II caused significant increase in cell size, reactive oxygen species and nitric oxide levels, inducible nitric oxide synthase (iNOS) and sodium-potassium ATPase ($Na^+/K^+$-ATPase) activities and protein expressions, as well nuclear factor kappa-light-chain-enhancer of activated B cell (NF-κB) expression. SNA209 and digoxin treatments significantly reduced these Ang II-induced changes. **Conclusion:** The effects of the SNA209 on the measured parameters were similar to that of digoxin. The compound SNA209 showed protective and inhibitory properties against Ang II-induced changes in H9c2 cardiomyocytes.

**P-9**

## Synthesis, Characterisation, Thermal Stability and Antimicrobial Activity of α-Mangostin and its Complexes with CU(II) and FE(II)

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**Introduction:** Xanthones have interesting structural scaffold and great variety of biological activities. Our ongoing interest in xanthones had driven us to look at the synthesis of metal complex by reacting our major compound, $\alpha$-mangostin with transition metal, Cu(II) and Fe(II). **Methods:** Both metal complexes, Cu(II)-$\alpha$-mangostin complex, $CuA_2(C_2H_5O)_2$ and Fe(II)-$\alpha$-mangostin complex, $FeA_2(CH_3O)_2$ had been synthesized successfully via one-pot reaction. The ligand and its metal complexes were characterized by 1D and 2D NMR Spectroscopy, UV-VIS, MS, CHNS and IR analysis. The thermogravimetric analysis measurement of the complex was performed by TGA and DSC. They were evaluated for their antimicrobial activity using Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC). **Results:** Synthesized ligand behaves as bidentate and coordinates to metal ion through oxygen atoms of carbonyl and hydroxyl. Based on the experimental data an octahedral geometry around the metal ion was assigned to both metal complexes. It was found that Cu(II) complex was thermally stable than Fe(II) complex. The thermal decomposition of metal complexes occurs in steps involving dehydration, melting and degradation processes. Cu(II)-$\alpha$-mangostin complex showed stronger inhibition against *Escherichia coli* at concentration 14.07 μg/mL as compared to $\alpha$-mangostin. The inclusion of iron metal has improved MIC value for Fe-$\alpha$-mangostin complex against *Pseudomonas aeruginosa* and *Klebsiella pneumonia*. **Conclusion:** The ligand and both metal complexes showed strong inhibition towards five bacteria tested.

**P-10**

## Proteomic Map of Cancer Cells Treated with *Catharanthus Roseus* Extract

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**Introduction:** The chemical extraction of *Catharanthus roseus* which is used in traditional herbal medicine has a role in cancer treatment and contributed significantly in the development of antileukemic drugs. **Methods:** The screening of the effect of this novel medicinal plant by using proteomic technology has been used to identify treatment related changes in cancer. Two-dimensional gel electrophoresis is one of the screening bioassays of separation for resolving complex mixtures of protein was used to determine treatment related changes in Jurkat cells treated with ethanolic *Catharanthus roseus* extract. **Results:** The separation of protein bands by one dimensional gel electrophoresis had produced 29 bands on the treated cells with

*Catharanthus roseus* in relative to the untreated cells that had shown 35 bands. Otherwise, with the use of two-dimensional gel electrophoresis, the spots of protein identified were 225 spots in treated cells as compared to 191 spots in the untreated cells. The results showed that the technique can detect variation in protein bands or spot in the treated and untreated cells. **Conclusion:** The implementation of this proteomic technology has enable its potential in defining precise molecular mechanism to look for the correlated protein of cancer cells and therefore will led to the development of specific diagnostic testing in particular disease. This procedure remains the most widely applied method in proteome analysis to elucidate cellular mechanism.

## P-11

## $P2Y_6$ Receptor Mediates Mechanoactivation of Survival Signal in Cardiomyocyte

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**Introduction:** Mechanical forces play important role in regulating structural and functional changes in mammalian cells especially cardiac cells. Mechanical stimuli sensed by cells through receptors and integrin are transmitted through cascades of intracellular signals that result in altered physiological responses or pathological condition. Pressure overload-induced cardiac cells remodeling underlie the pathogenesis of a variety of heart diseases, such as hypertension, maladaptive hypertrophy and consequently heart failure. It has been shown that Angiotensin type 1 receptor (AT1R) inhibition in cardiomyocyte attenuate mechanical stress-induced hypertrophic responses. In our previous research, we demonstrated that AT1R form heterodimer with $P2Y_6$ receptor ($P2Y_6R$) and each receptor play role in enhancing or attenuating each other functions. In this study, we aim to investigate role of $P2Y_6R$ in mechanical stretch-induced cardiomyocyte survival responses. **Methods:** Primary cardiomyocyte cells isolated from rat neonate heart were cultured on silicon-rubber culture chamber in Dulbecco Modified Eagle Medium (DMEM) supplemented with 10% Fetal bovine serum. Cultured cardiomyocyte were subjected to 20% mechanical stretch for certain duration of times and then harvested for MAPK protein measurement by western blot. The role of $P2Y_6R$ was investigated by treating the cell with $P2Y_6R$ specific inhibitor (MRS2578) prior to mechanical stretch**. Results:** Our finding shows that $P2Y_6R$ inhibition suppresses mechanical stress induced MAPK and AKT activation in cardiomyocyte. AKT is associated with activation of survival signaling in cells. **Conclusion:** These preliminary findings suggest that $P2Y_6R$ might be mediating an activation of survival signaling during mechanical stress.

## P-12

## The Effects of Different Compound Vehicles on Pregnant Rat Health Status

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**Introduction:** Vehicles used as delivery system for certain compounds in in vivo studies have been well established. However, their effect on the health status on pregnant subjects were scarcely studied. The vehicles itself could affect the pregnant subject used as they have slight changes in the vital health parameters during pregnancy. Although few studies have been conducted, there were neither detailed vehicle used nor formulation for pregnant rats. Therefore this study aims in elucidating the effects of different common vehicles used in delivering compound on the health status of pregnant Sprague Dawley (SD) rats. **Methods:** The pregnant rats were grouped into five and fed with drinking water containing various vehicles (Tween 80, methanol and acetonitrile) and concentration that able to dissolve BPA. The general health observation was noted throughout the gestational day (GD). Cardiomyocytes beating frequencies were also recorded and compared. **Results:** We observed there were changes in general health status of the pregnant rats however, the changes were not significant. We also determined that beating frequencies was not affected by solvents used ($p>0.05$), as well as other observation on weight, length and number of fetuses. Despite that, we could observed changes of physical appearance and drinking pattern in the rats. Interestingly, drinking patterns were found to be significant ($p<0.05$). **Conclusion:** The reduced water intake in pregnant rats with acetonitrile could be due to strong taste and smell of the vehicle compound in water compared to the other two vehicles. However, further investigation would be required to investigate the impact of solvents used as a vehicle or carriers in SD especially on liver toxicity.

## P-13

## Effect of Bisphenol A on the Intestinal Barrier

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**Introduction:** Bisphenol A (BPA) is a xenoestrogen chemical compound which is widely distributed throughout the environment. It is widely used to manufacture polycarbonate plastics used in infant feeding bottles, containers or table wares and as lining of food and beverage cans. BPA has wide range of harmful effects in different organs of the body. Although many organs of the body have been studied for the harmful effects of BPA, the first site of prolonged BPA exposure, the intestinal tract has received almost no attention. Intestinal mucosa acts as a barrier in between the

intestinal lumen and the internal organs and prevents different intestinal and extra intestinal harmful consequences in the body. It is not clear whether BPA induced harmful effects in the body occurs through disrupting the intestinal barrier (IB). Objective of this research was to have a comprehensive idea about the effect of BPA on the IB. **Methods:** Literatures were searched in pubmed, scopus and google scholar using the key words BPA paired with intestinal barrier, intestinal barrier function, gut barrier function, gut and intestinal permeability from the year 1980 till early March 2018. **Results:** A total of 40 articles were found. After exclusion of the duplicate studies and inclusion of the related one, only seven articles were retrieved. BPA was found to increase intestinal permeability, an indicator of compromised IB in one in-vitro study. But it dose-dependently decreased colonic permeability in one animal study. BPA has been reported to alter gut microbiota in five studies. Altered gut microbiota is proposed to be an important factor contributing to compromised IB. **Conclusion:** Well-designed larger studies are required to have a comprehensive data about the effect of BPA on the intestinal barrier.

## P-14

## Evaluation of Antiviral Effect and Possible Mechanism of Action Of 1-Substituted 5-(Phenylamino)Uracil Derivatives against Chikungunya Virus

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**Introduction:** Chikungunya virus (CHIKV) infection is one of the most important and serious arbovirus infections in Malaysia. CHIKV infection has been associated with chronic arthritis and cause severe morbidity. N- substituted 5-(phenylamino)uracils derivatives have shown effectiveness against HIV, Hepatitis C and other RNA viruses, however, their antiviral effect against CHIKV remains unknown. This study aimed to evaluate the potential of 11 N-substituted 5-(phenylamino)uracils derivatives against CHIKV. **Methods:** Primary screening of 11 tested compounds on Vero cells in a 96 well plate was done on CHIKV at 48 hrs with doses ranging from 1.25 uM to 100 uM with a MOI of 1. Compounds which showed inhibitory effect were subjected to time-of-addition assay. The supernatant from treated, virus control and cell control groups were collected and subjected for real-time RT-PCR to determine RNA copy number, and virus plaque assay was done to indicate the exact time point of inhibition. Then, proteins from treated groups, virus control group and cell control group were subjected for 2D gel electrophoresis and the differentially expressed protein spots were extracted for mass spectrometry analysis to identify the proteins involved in inhibitory effect. **Results:** Compounds Z214 and Z364 were found to have inhibitory effect against CHIKV. Time-of-addition assay showed inhibitory effect for both compounds at 4-6 hrs post infection with significant reduction of RNA copy number. The virus plaque assay at 6hour post infection showed significant reduction of virus plaque formation in treated group as compared to virus control group. The mass spectrometry revealed protein annexin A2 and peroxiredoxin-1 were upregulated in treated groups compared to virus control group. **Conclusion:** Z214 and Z364 both produced anti-CHIKV effect at post

infection stage and that is probably associated with their host-modulating action on reactive oxidative stress by upregulation of annexin A2 and peroxiredoxin 1 in host cells.

## P-15

## Nisin ZP Has a Better Potential as an Anti-Cancer Agent against Osteosarcoma Compared to Nisin

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**Introduction:** Nisin, one of the oldest and safest lantibiotics, is now being explored for its use as anti-cancer agent. Recent studies showed promising results for Head and Neck cancer. The treatment for osteosarcoma, a difficult to treat bone cancer with high recurrence, hasn't been changed much during the last 10 years. In this study we wanted to compare the cytotoxicity of two Nisin mixtures: Nisin and Nisin ZP against MG63 osteosarcoma cells. **Methods:** Nisin (Gold Biotechnology) and Nisin ZP (Hardary SA) were solubilized followed by serial dilution to obtain 0 - 4000 µM. Approximately 6000 MG-63 cells/well were seeded and incubated with either Nisin or Nisin ZP for 48 hr. The cell viability was determined using MTS assay while morphological changes were observed using an inverted light microscope at 10x, 20x and 40x magnifications. **Results:** Both Nisin preparations caused cell death in osteosarcoma cells, however the $IC_{50}$ for Nisin ZP was significantly lower (700µM) than for Nisin (3000µM). Microscopic images demonstrated that MG-63 cells underwent cell death with evidence of cell rounding, apoptotic bodies and blebs. The difference in activity between Nisin (Gold Biotechnology) and Nisin ZP (Hardary SA) seems to be due to either purity and/or variants of the Nisin used. Among the 8 natural variants of Nisin, the A, Z and P variant have shown anti carcinogenic properties. **Conclusion:** Our results indicate that the NP variants are more potent than the Nisin mixture however further studies have to be conducted to explore the reasons for this difference in potency.

**P-16**

## Ameliorative Effect of Procyanidin-C1 on Spermatogenesis in Bisphenol-A Induced Aged Mice

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**Introduction:** Advanced paternal age has been associated with infertility due to the increase of oxidative stress in the male reproductive system. Bisphenol-A (BPA) is an endocrine-disrupting chemical which is widely used in the production of polycarbonate plastics. It has been shown to impair spermatogenesis. In contrast, procyanidin C1 (PCY-1), an antioxidant from *Vitis vinifera L.* has been shown to have antiviral, antimelanogenic activity and immunostimulatory effect. We hypothesize that PCY-1 is able to ameliorate the adverse effect of BPA in spermatogenesis. The objective of this study was to evaluate the effect of PCY-1 on spermatogenesis of BPA-treated aged mice. **Methods:** Male C57BL/6 mice aged 20 months were divided into 4 groups (n=6). Males in the four groups were treated with ultrapure water (control), BPA (15mg/kg/bw), PCY-1 (20µg/kg/bw) and BPA 15mg/kg with 20 µg/kg of PCY-1 respectively, for 35 days. The cauda epididymis and testes were collected on Day-36, for sperm parameter analyses and histomorphometry. Statistical significance was determined by one-way ANOVA with $p<0.05$ **Results:** In sperm parameter analyses, compared to control, PCY-1 treatment significantly improved sperm morphology (27.16±1.14 vs. 48.83±1.30) and sperm count (54.00±1.41 vs. 69.00±1.41). In addition, compared to BPA treatment alone, BPA+PCY treatment significantly improved sperm morphology (9.33±2.66 vs. 26.5±10.13) and sperm count (34±1.41 vs. 52.0±2.83). Histomorphometry showed that compared to control, PCY-1 treatment significantly increased seminiferous tubule diameter (49.621±1.190µm vs. 63.50±1.17µm) and epithelial height (28.388±0.835 µm vs. 45.55±1.01µm). Meanwhile, compared to BPA treatment, BPA+PCY-1 treatment significantly increased seminiferous tubule diameter and epithelial height (37.707±1.093µm vs. 46.08±1.60µm, 20.541±0.818µm vs. 28.95±1.13µm) **Conclusion:** In conclusion, PCY-1 enhances spermatogenesis in aged male mice exposed to BPA.

## P-17

## Modification of Chitosan Biopolymer: An Approach to Improve Blood Purification Membrane Hemocompatibility

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**Introduction:** Chitosan is a non-toxic, biodegradable and biocompatible natural polymer that is commonly found in arthropods exoskeleton, fungi cell wall and yeast. Currently, chitosan biopolymer has been widely used in many biomedical applications due to its excellent physical and chemical properties. However, the cationic surface and the amino group of the chitosan might cause blood clotting which makes it unsuitable to be used in blood-contacting applications such as blood purification. Membrane is employed as a medium for extracorporeal blood purification process to remove the toxins and waste from blood. The hemocompatibility of the blood-contacting membrane material is essential in order to avoid blood coagulation. **Methods:** Several approaches have been reported to modify the chitosan to become more hemocompatible for blood-contacting materials. This paper highlights the methods that has been used for the modification of chitosan to enhance its hemocompatibility. Besides, the incorporation of hemocompatible chitosan in the fabrication of hemocompatible membrane for blood applications especially hemodialysis will also be discussed. **Conclusions:** The enhanced hemocompatible chitosan and chitosan-modified membranes has shown to be a promising material for future biomedical applications particularly for blood-contacting application.

## P-18

## Acid-Functionalized Activated Carbon for Creatinine Adsorption

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**Introduction:** The poor dispersion of activated carbon (AC) limits its use in medical applications. In hemodialysis, AC is sometimes embedded in membrane or used separately in an integrated sorbent cartridge in the form of suspension to adsorb uremic toxins. This study attempts to functionalize AC and compare its creatinine adsorption properties with that of pristine AC. **Methods:** Chemical oxidation was performed on AC using a concentrated nitric acid, forming acid-functionalized AC (AC-COOH). Creatinine adsorption study was conducted on the two adsorbents, where the effects of pH, initial concentration and contact time were investigated. **Results:** It was

found that AC-COOH readily dispersed in water. There was no significant difference on the removal efficiency of creatinine at different pH. The creatinine adsorption by AC-COOH was rapid in the first 2 h with 1.5 times the rate of the pristine AC. Within the first 4 h, it adsorbed creatinine at a much faster rate. Nevertheless, it achieved equilibrium at 7 h with the adsorption capacity of 90.8 mg/g, whereas the pristine AC had a higher adsorption capacity (96.7 mg/g) after 17 h. **Conclusions:** The improved dispersion and the enhanced adsorption kinetics made AC-COOH suitable for 3-4 h hemodialysis operation.

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## Challenges in Removal of Protein Bound P-Cresol Sulphate

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**Introduction:** Uremic toxin p-cresol is an end-product of protein catabolism. It is a small molecule that is more than 90% bound to plasma proteins. Healthy kidney removes p-cresol from the body by tubular secretion. However, this function is not achievable in conventional haemodialysis. Free, unbound solute can diffuse easily across the membrane of haemodialysis, but clearance by conventional haemodialysis for p-cresol is limited which resulted in accumulation of p-cresol in the body. Accumulation of p-cresol have been associated not only in the progression of chronic kidney disease (CKD), but also in the development of cardiovascular disease in haemodialysis patients. Thus, many studies were done on how to remove the protein bound uremic toxins. High flux haemodialyser, hemoperfusion and fractioned plasma separation have been developed recently to enhance the removal of p-cresol. However, the problem is still unresolved, p-cresol is still independently associated with mortality. The purpose of this short review is to discuss the current technologies for the removal of p-cresol and future development in improving the removal of this uremic toxin. **Methods:** Each method of removal of p-cresol was detailed, along with the biocompatibility properties of the materials used for the filtration of p-cresol. **Conclusion:** This short review is performed with the hope to help researchers to understand the challenges and current approach in removal of p-cresol uremic toxin.