JOURNAL OF CLINICAL AND HEALTH SCIENCES

JCHS

SUPPLEMENTARY ISSUE

MARCH 2024
VOLUME 9 ISSUE 1 (SUPPLEMENTARY)

INTERNATIONAL CONFERENCE ON PRECISION HEALTH IN THE INDUSTRIAL REVOLUTION (IR)

"Precision Healthcare : From Research to Practice"

26-30 AUGUST 2023

Organized by :

Malaysian Metabolomics Society (MyMS)
(PPM-003-10-29072011)

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UNIVERSITI TEKNOLOGI MARA

Hospital Al-Sultan Abdullah

INTERNATIONAL CONFERENCE ON PRECISION HEALTH IN THE INDUSTRIAL REVOLUTION 4.0 (IC-PHIR)
26-27TH AUGUST 2023

Venue: Hospital Al-Sultan Abdullah,
Universiti Teknologi MARA,
42300 Bandar Puncak Alam,
Selangor

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KS 01
REVOLUTIONIZE DIAGNOSIS AND MANAGEMENT OF RARE AND NEUROLOGICAL DISEASES: THE CHALLENGES

Prof. Dr. Teh Lay Kek

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Rare diseases present intricate diagnostic challenges, particularly within diverse populations like Malaysia. Malaysia's genetic diversity, stemming from its multicultural makeup, underscores the urgency of transforming rare disease diagnosis. Conventional diagnostic methods often fall short in uncovering the genetic variants responsible for these conditions, leading to misdiagnoses or diagnostic delays. Recognizing the potential of innovative approaches is crucial for addressing this gap. Transforming rare disease diagnosis necessitates the collaboration of multiple stakeholders. Collaborations between research institutions and private companies can drive innovation, making advanced diagnostics more accessible and affordable, while government entities provide policy frameworks and funding support. Policy initiatives can incentivize private sector involvement in rare disease research and diagnostics. Funding for research, infrastructure development, and training programs can facilitate the integration of genomic insights into clinical practice. Regulatory frameworks can ensure the ethical and responsible use of genetic information while protecting patient rights and privacy. On successful example of such endeavor is the 100,000 Genomes Project, a partnership between the government, National Health Service, and private companies, aimed to sequence 100,000 genomes from patients with rare diseases and cancers. This initiative had revolutionized diagnostics and personalized treatments. In 2023, a group of clinicians and researchers in Malaysia have come together in collaboration to set up the Consortium of Genomics for Rare and Neurological Diseases with a shared vision of improving patient outcomes and healthcare quality of patients with rare and neurological diseases. The main focus of the consortium is to use Next-generation sequencing (NGS) platform in the quest to identify elusive genetic variants responsible for rare diseases. The ability to uncover intricate genetic variations, especially within the context of a diverse population, holds immense promise for accurate diagnosis, novel therapeutic avenues, and enhanced patient care. We believed that by harnessing the collective strengths of all stakeholders, Malaysia can revolutionize diagnosis and management of rare and neurological disease, improving the lives of affected individuals and families.

Keywords: Rare disease, neurological diseases, Next-generation sequencing (NGS)

PS 01

EMBRACING BIOMEDICAL OMICS RESEARCH FOR PRECISION HEALTH INITIATIVES IN MALAYSIA

Prof. Dato' Dr. Mohd Zaki Salleh

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The integration of cutting-edge Biomedical Omics research, stands as a pivotal catalyst driving transformative Precision Health Initiatives within Malaysia. This exploration delves comprehensively into the crucial and dynamic role of Biomedical Omics technologies – encompassing genomics, proteomics, metabolomics, and more – in a paradigm shift that is reshaping the entire healthcare landscape of the nation. At the heart of these advancements lies the intricate dissection of individual biological data at a molecular level, a feat that has been realized through research efforts at iPROMISE UiTM. These endeavors have primed Malaysia's Precision Health Initiatives with a powerful platform for significant leaps forward in personalized healthcare solutions. Central to the narrative is the fusion of state-of-the-art technologies, advanced data analysis methodologies, and a culture of interdisciplinary collaboration. Together, these elements synergize to propel the implementation of highly tailored medical interventions, proactive disease prediction models, and innovative health promotion strategies. However, the impact does not stop at the laboratory doors. This dynamic research journey from iPROMISE UiTM finds a practical conduit to the public through the dedicated efforts of Zakesy Biotech S/B, a startup company poised at the intersection of scientific innovation and commercial services. The translation of this research into real-world applications has accelerated the transformation of Precision Health from concept to tangible reality. The seamless transition of research from iPROMISE UiTM to commercial initiatives by Zakesy Biotech S/B demonstrates the impacts of embracing Biomedical Omics Research and the commercially viable healthcare paradigms.

Keywords: Biomedical Omics, personalized healthcare, precision health

PS 02

PRECISION HEALTH AND GENOMICS: THE INTERSECTION OF SCIENCE AND MEDICINE

Dr. Ong Seng Kai

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Precision health, the practice of customizing medical treatment to an individual's specific needs based on their genetic, environmental, and lifestyle factors, has gained significant momentum in recent years. Genomics, the study of an individual's entire genetic makeup, has played a critical role in enabling precision health. In this talk, I will explore the intersection of genomics and precision health and how genomics can provide insights into disease prevention, diagnosis, and treatment. I will discuss the latest advances in genomics research, including the use of genome-wide association studies, next-generation sequencing, and functional genomics. I will also highlight the current technical challenges associated with integrating genomics into precision health, such as complexity of a polygenic trait, data interpretation and the heterogeneity problem. Finally, I will share my insights on the future of precision health and genomics and how this field is likely to transform medicine and improve patient outcomes. This talk will provide valuable information and insights for researchers, clinicians, and policymakers interested in precision health and genomics.

PS 03
PHARMACOGENOMICS AND PRECISION MEDICINE THIOPURINE AND BEYOND

Dr. Jun J. Yang

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This talk delves into the intersection of genomics and cloud computing, shedding light on the immense potential it holds for advancing precision medicine. By focusing on the synergies between these two fields, we aim to inspire researchers, clinicians, and industry professionals to harness the transformative power of genomics data analysis in healthcare. The discussion will encompass the challenges faced in managing, analysing, and interpreting genomic data, and explore how cloud computing, with its scalability and analytical capabilities, can provide innovative solutions. Real-world examples will be shared, highlighting the impact of this convergence on personalized treatment options and patient outcomes. Attendees can expect to gain insights into emerging trends, best practices, and the future prospects of genomics and cloud computing in revolutionizing precision medicine.

PS 04

PRECISION DENTAL HEALTHCARE: A PERSONALIZED APPROACH TO DENTAL CARE

Prof. Dr. Rohana Ahmad

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Precision Dental Healthcare marks the beginning in a new era of personalized treatment as technology evolves and is integrated into healthcare. This approach moves away from the traditional one-size-fits-all model and toward a tailored strategy that takes genetics, lifestyle, and environmental factors into account. Genomic insights offer valuable information regarding a patient's predisposition to certain dental conditions, such as enamel degradation, periodontal disease, bone resorption or orthodontic relapse. While the potential benefits of this approach are considerable, it is imperative to navigate challenges, particularly those related to the ethical use of genetic data and economic implications. As the methodology matures, and with thoughtful consideration of its intricacies, precision dental healthcare has the potential to redefine the standard of dental care, elevating both patient outcomes and professional practices.

PS 05

NANO-ORGANOTHERAPY: PRECISION MEDICINE WITH ORGAN-SPECIFIC NANO-PEPTIDES

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Organotherapy is a field of medical practice that uses animal origin organ extracts to treat the same organs in human. This therapeutic modality has gone through a long history from the empirical use of organ-specific extracts in antiquity to the use of nano-sized peptides today. The main features of organotherapy are the use of a mixture of the active ingredients; all active ingredients are derived from a natural source; the used concentration and combination of the active ingredients correspond to the natural concentration and combination of these substances in a healthy organ. Since the effectiveness of any treatment depends on the competence of the physician, so, the more knowledgeable and experienced the doctor who practices organotherapy, the higher the expected therapeutic effect, and the greater the likelihood that the treatment can be attributed to "Precision Medicine".

PS 06
DECIPHERING RARE AND UNDIAGNOSED DISEASES: WHAT'S MISSING MATTERS

Dr. Jawahar Swaminathan

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Oxford Nanopore Technologies (ONT) offers a fast, simple, accurate and scalable genomic sequencing solution for use in rare and undiagnosed diseases. ONT sequencing is capable of identifying all genomic variation ranging from complex chromosomal rearrangements, copy-number variants and structural variants to tandem-repeat disorders, SNPs and inDels. A major differentiator for ONT sequencing compared with short-read technologies includes the ability to read "dark regions" of the genome where many disease-causing genes are known to be present. In addition, our sequencing solutions can detect epigenetic modifications (methylation) on the genome with unparalleled accuracy and speed. Taken together, ONT sequencing can replace all existing genomic technologies and offer accurate results in a speedy manner. My presentation today will focus on how ONT is being used to gain deeper insights into rare and undiagnosed diseases with real-life examples from publications.

ORAL PRESENTATIONS

<u>OP 01</u>
TOTAL KAURENOIC ACID, ANTIOXIDANT CAPACITY, AND ANTIMELANOGENIC ACTIVITY OF ADENOSTEMMA LAVENIA LEAVES

<u>Anisya Elsa Shafira</u>[1], Rifan Nurfalah[1], Sandra Arifin Aziz[2,3], Taopik Ridwan[3], Muhammad Farid[1], Hiroshi Takemori[4,5], and Irmanida Batubara[1,3*]
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INTRODUCTION: *Adenostemma lavenia (*Asteraceae) is a medicinal plant, commonly seen as weed spread across Pakistan, India, China, Taiwan, and almost all Southeast Asia. The leaf extract of *A. lavenia* has been reported to contain high level of *ent-11α-hydroxy-15- oxo-kaur-16-en-19-oic acid* (11αOH-KA, kaurenoic acid class), which exhibits antioxidant and anti-melanogenic activities. This study aimed to determine the total kaurenoic acid, antioxidant capacity, and anti-melanogenic activity of *A. lavenia* leaves extract. **METHODS:** One (1) gram of dried leaves harvested from *A. lavenia* was soaked with methanol at 1:20 (w/v) ratio for 3 hours. The extract was dried, and its antioxidant capacity was measured using 2,2-diphenyl-1-picrylhydrazyl (DPPH) test. The melanin content of the extract was estimated using the anti-melanogenic assay in mouse melanoma cells (B16F10). The total kaurenoic acid (KA) was analyzed using the high-performance liquid chromatography (HPLC) method. **RESULTS:** The antioxidant capacity was 8.98 ± 1.73 µmol AAE/g dried leaf. Meanwhile, the anti-melanogenic assay revealed that the extract of *A. lavenia* at concentration of 5 and 10 µM exhibited better inhibition compared to the extract at a concentration of 15 µM. **CONCLUSION:** Therefore, *A. lavenia* has the potential to be an antioxidant and it shows dose-dependent inhibition of anti-melanogenic property at doses ranged from 5 to 10 µM. Further, the extract was found to contain 9.36 ± 0.99 mM of KA in one gram of dried leaf. The methanol extract of *Adenostemma lavenia (*Asteraceae) is a potential component for cosmetic products with antioxidant and anti-melanogenic properties. However, further study is required to understand the safety, efficacy and pharmacokinetic properties of the active compounds in the extract.

Keywords: Anti-melanogenesis; Antioxidant; DPPH; *ent-11α-hydroxy-15- oxo-kaur-16-en-19-oic acid*; HPLC

OP 02
TOTAL KAURENOIC ACID, ANTIOXIDANT CAPACITY, AND ANTIMELANOGENIC ACTIVITY OF KAURENOIC ACID OF ADENOSTEMMA PLATYPHYLLUM

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INTRODUCTION: *Adenostemma*, a medicinal plant belonging to the Asteraceae family, has gained significant attention due to its rich phytochemical profile and potential therapeutic properties. Terpenoids are a class of compounds found in many medicinal plants, including *Adenostemma platyphyllum*. Terpenoids encompass a vast array of compounds due to their structural diversity, which arises from different arrangements and modifications of isoprene units, causing terpenoids to exhibit a remarkable variety of biological functions, including antimicrobial, antiviral, anticancer, anti-inflammatory, antimelanogenic, and antioxidant activities. Another species of *Adenostemma*, *A. lavenia*, was reported to contain high levels of the diterpenoid compound, kaurenoid acid, ent-11α-hydroxy-15- oxo-kaur-16-en-19-oic acid (11αOH-KA), which is efficacious for antioxidant and antimelanogenic. This work aims to observe the potential use of *A. platyphyllum* as an antioxidant and antimelanogenic agent. **METHODS:** Kaurenoic acid was isolated using water extraction followed by chloroform distribution. Using the HPLC method, the isolated 11αOH-KA was used as the standard to determine the total kaurenoic acid level of *A. platyphyllum*. The antioxidant capacity of *A. platyphyllum* was determined using a 2,2-diphenyl-1-picrylhydrazyl (DPPH) method. The antimelanogenic effect was investigated using mouse melanoma cells (B16F10) responsible for melanin synthesis as the experimental model. **RESULTS:** The 11αOH-KA level in *A. platyhyllum* extract was 0.200 ± 0.007 µmol/mL. The antioxidant capacity of the extract was 0.320 ± 0.094 µmol/mL. Meanwhile, the highest concentration of the extract which showed the highest antimelanogenic activity was 15 µg/mL. **CONCLUSION:** *A. platyphyllum*, exhibited remarkable antimelanogenic and antioxidant abilities. Extensive research has demonstrated the potential of *A. platyphyllum* extracts and their bioactive compounds as antioxidant and antimelanogenic agents, attributed to their rich phytochemical profile, including terpenoid, especially kaurenoic acid.
Keywords: *Adenostemma platyphyllum*, antioxidant capacity, antimelanogenic, isolation, kaurenoic acid, terpenoid.

<u>OP 03</u>

LCMS-MS-BASED METABOLOMICS AND IN SILICO ANTIBACTERIAL OF THREE ADENOSTEMMA SPECIES

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INTRODUCTION: Three *Adenostemma* species, *Adenostemma lavenia* (AL), *A. madurense* (AM), and *A. platyphyllum* (AP), were selected for this work as they are the most reported *Adenostemma* species. Folk medicine has traditionally employed its leaves and entire plants to treat fever, inflammation, and lung damage. Therefore, this study aimed to identify specific metabolite profile for each species. **METHODS:** UHPLC-Q-Orbitrap HRMS was used to profile the chemical features for each extract, multivariate statistical analyses were conducted to identify the significant chemical features and *in-silico* molecular docking was done to identify compounds of *Adenostemma* with antibacterial properties. The leaf samples were extracted using sonication with methanol, filtered, and analyzed. **RESULTS:** Thirty-five compounds were identified based on their masses and fragmentation characteristics. Most compounds were first reported in the *Adenostemma* genus. The PCA model exhibited separate clusters for the three species, confirming substantial chemical differences between their extracts. The HCA dendrogram and heatmap revealed that the AL metabolites profiles are closer to those of AM than AP. Flavonoids and alkaloids were abundant in AL*,* while phenolic acids and flavonoids were mainly contained in AM. In contrast, phenolic acids, aliphatic acids, and fatty acids were the primary metabolites identified in AP*.* The molecular docking revealed that pectolinarigenin and eriodictyol 7-O-sophoroside (the major compounds of *A. lavenia*) and dicaffeoylquinic acid (high in abundance in *A. platyphyllum*) have the highest binding affinity to the bacterial protein targets (*S. aureus* UDP-GlcNAc 2-epimerase, *E. coli* UDP-3O-(3-hydroxymyristoyl) glucosamine N-acyltransferase*,* and *P. aeruginosa* pyochelin synthase PchD). **CONCLUSION:** This study revealed that integrating metabolomics and in-silico approaches are fast screening methods for metabolites discovery. Furthermore, this preliminary research is a continuous effort in bioprospecting the *Adenostemma* as a medicinal plant with antibacterial potential.

Keywords: *Adenostemma*, chemical profiling, health, medicinal plant, molecular docking

OP 04

REVITALIZING THE MIND AND BODY: UNVEILING THE IMPACT OF EXERCISE INTERVENTION IN UNIVERSITY STUDENTS ON PSYCHOLOGICAL WELL-BEING, BDNF LEVELS, AND SERUM METABOLOMICS

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INTRODUCTION: Physical activity is widely acknowledged for promoting psychological well-being among university students. This study aimed to investigate the impact of exercise intervention on the levels of stress, anxiety, and depression (SAD), serum metabolomics profiles as well as brain-derived neurotrophic factor (BDNF), among the university students. **METHODS:** Forty participants underwent an 8-week moderate-intensity aerobic physical activity following the WHO guidelines. The Depression, Anxiety, Stress Scale 21 (DASS-21) was used to assess the severity of SAD in university students pre-and post-intervention. Morning serum samples were collected before and after the intervention to measure BDNF levels and Liquid Chromatography Mass Spectrometry-Quadrupole Time of Flight (LCMS-QTOF) analysis was performed to assess changes in metabolite profiles. **RESULTS:** Participation in physical activity was associated with a decrease in SAD levels. Furthermore, the expression of 119 metabolites which mapped to 28 biological pathways were changed post intervention ($p < 0.05$ and FC>2). The results showed significant alterations in serum metabolites related to pantothenate and CoA biosynthesis and glycerophospholipid metabolism. Moreover, an improvement in BDNF levels was observed post-intervention. **CONCLUSION:** These findings highlight the potential of LC-MS-QTOF-based serum metabolomics to uncover the metabolic changes induced by exercise interventions, including the modulation of BDNF. Understanding these changes, particularly in BDNF levels, provides valuable insights into the underlying mechanisms of exercise-induced psychological and health benefits, such as neuroplasticity and cognitive function enhancement, and aids in the development of personalized exercise programmes to promote overall well-being.

Keywords: Brain-Derived Neurotrophic Factor (BDNF), Physical activity, Stress; anxiety and depression (SAD).

OP 05

HLA-B*15:02, HLA-B*15:13 AND HLA-B*15:21 ALLELES AND THE RISK OF CUTANEOUS ADVERSE DRUG REACTIONS ASSOCIATED WITH THE USE OF CARBAMAZEPINE, PHENYTOIN AND LAMOTRIGINE AMONG THE MALAYSIAN POPULATION

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INTRODUCTION: Genetic polymorphisms of the *HLA* alleles are among the risk factors for the incidence of cutaneous adverse drug reactions (CADRs) induced by antiepileptics. The aim of the study is to determine the association between three *HLA-B* alleles (*HLA-B*15:02*, *HLA-B*15:13*, and *HLA-B*15:21*) and the risk of CADRs, including Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), among Malaysians. **METHODS:** This case-control study included patients treated with carbamazepine, phenytoin, or lamotrigine in three public hospitals. *HLA-B*15:02*, *HLA-B*15:13*, and *HLA-B*15:21* genotyping was performed using the polymerase chain reaction-sequence specific primer method (PCR-SSP). **RESULTS:** A total of 88 patients (38 cases, 50 controls) were recruited, with a mean age of 35.1 ± 12.6 years. Carbamazepine was used by 59.1% of patients, followed by phenytoin (33%) and lamotrigine (31.8%). Among cases, 52.6% developed SJS, 5.3% developed TEN, 2.6% developed SJS-TEN, and 7.9% developed Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Allele frequencies for *HLA-B*15:02*, *HLA-B*15:13*, and *HLA-B*15:21* were 0.21, 0.09 and 0.07, respectively. Analysis for all three antiepileptic drugs as a group suggest that patients with *HLA-B*15:02* allele were 6.55 times more likely to develop CADRs, while the odds increased to 16.8 times when we include only severe reactions (i.e., SJS, TEN). Allele *HLA-B*15:13* was not found to cause an increased risk for CADRs, while the *HLA-B*15:21* allele showed an increased odds of 1.94 times for developing severe reactions, however, the association failed to reach significance due to low allele frequency. **CONCLUSION:** *HLA-B*15:02* allele is associated with an increased risk of developing CADRs, especially severe reactions. The *HLA-B*15:21* allele also shows potential risk, but larger studies are needed to confirm the association.

Keywords: HLA genotyping, SCAR, antiepileptics, pharmacogenomics, PCR-SSP

OP 06

FABRICATION OF ELECTRODE FOR A RAPID AND SENSITIVE APTAMER-BASED GLIADIN SENSOR

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INTRODUCTION: Gliadin is one of the primary proteins in gluten that can cause negative effects upon consumption by patients that are diagnosed with gluten-associated disorders such as celiac disease, dermatitis herpetiformis, gluten ataxia, gluten sensitivity, and gluten allergy. The only effective treatment for these types of patients is by practicing gliadin-free diet (GFD) that requires sensitive measurement of gliadin content in daily food consumption. Hence, the presence of an analytical tool that can precisely detect the amount of gliadin in food is useful to improve patient care. An aptamer-based electrochemical biosensor is most preferred due to rapid detection, high sensitivity, and cost-effective. **METHODS:** In this study, a simple aptamer-based electrochemical gliadin sensor was fabricated using self-assembly monolayers (SAM) formation technique. The aptamer was immobilized onto the working platform through interaction between the sulphur atom from thiol-modified Gli4 aptamer and the gold atom from the working electrode of a screen-printed gold electrode (SPGE), forming a strong covalent bond. The remaining free sites were blocked with bovine serum albumin (BSA) to prevent any non-specific binding during target analyte detection. Cyclic voltammogram (CV) and electrochemical impedance spectroscopy (EIS) were used to evaluate the fabricated electrode. **RESULTS:** Good linear range of detection between 0.01 to 1 ppm of gliadin was obtained. **CONCLUSION:** The fabricated sensor meets the lowest detection sensitivity as per FDA guideline for the detection of gliadin in food.

Keywords: Aptamer; Biosensor; Electrochemical; Gliadin

OP 07

ELECTROCHEMICAL STUDIES OF BIOSENSOR FOR GLUTEN DETECTION: A REVIEW

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INTRODUCTION: Gluten intolerance is likely to be caused by an inappropriate immune response toward gliadin, a fraction of gluten protein. Gluten intolerance has raised concern in a clinical setting due to its potential association with chronic inflammation that leads to diseases. Therefore, it is essential to be able to detect individuals at risk of gluten intolerance early. Conventionally, gluten is detected using enzyme-linked immunosorbent assay (ELISA) to capture the desired gluten analyte and quantify gluten concentration by color change. However, it is time-consuming and needs a specialist to handle the antibodies. Hence, a new biosensor that rapidly detects gluten with high sensitivity and easy to operate is desirable. Aptamer which is used in aptasensor is a short single-stranded DNA or RNA sequences for detection of desired targets. The chemical synthesis of aptamers offers high accuracy and reproducibility and allows chemical modifications to increase the substrate binding affinity. This study aims to review the electrochemical effect of the material on signal transduction, detection, and amplification towards the quantification and analysis via the application of the aptamer-based biosensor technique. **METHODS:** Electrochemical studies are a crucial part in the design, optimization, and evaluation of biosensors application for rapid, sensitive and selective detection and quantification of analytes. **RESULTS:** It was found that carbon nanomaterial, gold nanomaterials, and magnetic nanoparticles have high potential due to their characteristics like high surface-to-volume ratio, good conductivity, electrochemical activity, and ease of functionalization. Aptasensor coupled with nanomaterials are believed to have high sensitivity, stability, and user friendly to the patients or carers. **CONCLUSION:** Nanomaterials facilitate the immobilization of biomolecules of electroactive catalyst and results in amplified ultrasensitive electrochemical detection signal.

Keywords: Aptasensor, electrochemical, gluten, celiac disease

OP 08

INTEGRATING NUCLEAR MAGNETIC RESONANCE AND PHARMACOMETABONOMICS APPROACH TO PREDICT GENTAMICIN-INDUCED NEPHROTOXICITY IN SPRAGUE DAWLEY RATS

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INTRODUCTION: The antibiotic gentamicin has been extensively used, but its nephrotoxicity has been a major concern. Currently, there are no reliable metabolites that can be used as biomarkers for early detection. This study aimed to establish a pre-dose predictive model of gentamicin-induced nephrotoxicity. **METHODS:** Gentamicin was subcutaneously administered to induce nephrotoxicity in a group of Sprague-Dawley (SD) rats. Blood and urine samples were collected before, and after the treatment, and the kidney's histopathology was examined after the rats were sacrificed. Next, nuclear magnetic resonance (NMR) spectroscopy and a pharmacometabonomic approach were employed to investigate the differentiated metabolic pattern in serum and urine samples prior to the administration of gentamicin and a pre-dose predictive model was constructed. **RESULTS:** Gentamicin caused toxic responses in some SD rats (the toxic group) but had little effect in others (the nontoxic group), based on their clinical chemistry for nephrotoxicity and histological findings. The multivariate statistical analysis using orthogonal partial least-squares discriminant analysis revealed a significant distinction between toxic and non-toxic SD rats in terms of pre-dose metabolites. The data fitness and prediction ability of the pre-dose predictive models diverged. However, the pre-dose predictive models had good to fair accuracy (AUROC) with degrees of 0.7 and onwards. The pre-dose serum metabolites of interest were lactate, trimethylamine-N-oxide, xylose, deoxyinosine, 2-phosphoglycerate, and glucose-6-phosphate. The pre-dose urine contained 4-pyridoxic acid, 2-oxoglutarate, citrate, betaine, hippuric acid, allantoin, and urea among other metabolites of interest. **CONCLUSION:** These results indicate that the models of the pharmacometabonomic approach may be useful for predicting gentamicin-induced nephrotoxicity prior to dosing.

Keywords: gentamicin, nephrotoxicity, pharmacometabonomic, NMR fingerprinting

OP 09

THE GENETIC VARIABILITY OF UDP-GLUCURONOSYLTRANSFERASES (UGTS) AMONG THE MALAYS AND ORANG ASLI IN MALAYSIA: IMPLICATION IN VARIABLE DRUG METABOLISM AND DETOXIFICATION

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INTRODUCTION: UDP-glucuronosyltransferases (UGTs) are a vital group of enzymes responsible for the biotransformation of numerous endogenous and exogenous compounds. UGTs play a critical role in drug metabolism and detoxification processes. **METHODS:** This study examines the genetic diversity of 14 UGT enzymes using population-scale sequencing data from 96 individuals of the Malays and 105 individuals of the Orang Asli who identified themselves as healthy. **RESULTS:** The Malays showed a total of 5447 genetic variants, including 2942 intronic and 2505 exonic variants. Among the variants, there were 190 synonymous, 313 missense, 84 3'UTR, 31 5'UTR, 14 stop-gain, 9 splice region, 408 downstream, 1443 upstream, 12 intergenic, and 1 splice donor. On the other hand, the Orang Asli also displayed 5447 genetic variants, with 2930 being intronic and 2517 exonic variants. Among the exonic variants, there were 118 synonymous, 181 Missense, 53 3'UTR, 25 5'UTR, 2 stop-gain, 9 splice region, 488 downstream, 1632 upstream, 8 intergenic, and 1 splice donor. Overall, both populations showed 206 low impact variants, 369 moderate impact variants, 16 high impact variants, and 7414 variants with modifier roles. The significance of UGTs in drug metabolism cannot be overstated, as they have a substantial influence on the pharmacokinetics of drugs. Their functionality directly impacts drug clearance rates, bioavailability, and potential drug-drug interactions. UGTs' play vital roles in detoxification processes, safeguarding the body from harmful substances encountered through dietary intake, environmental exposure, and the breakdown of endogenous compounds. Dysfunction or genetic polymorphisms in UGT genes can lead to impaired detoxification, potentially leading to the onset of certain diseases or increased vulnerability to toxicity. **CONCLUSION:** Understanding the complexities of UGT-mediated processes provides valuable insights into specific ethnic drug responses and opens opportunities for advancements in personalized medicine and pharmaceutical research.

Keywords: drug response, genetic polymorphism, precision health.

OP 10

THE GENETIC ANALYSES OF MAJOR CYTOCHROME P450 ENZYMES AMONG THE MALAYS AND ORANG ASLI IN MALAYSIA

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INTRODUCTION: Cytochrome P450 (CYP) exhibits significant genetic diversity, with numerous isoforms identified. Each isoform displays distinct substrate specificity, leading to variation in drug response among individuals. Understanding the genetic polymorphisms and allelic variations in CYP genes is of paramount importance in personalized medicine and drug development. **METHODS:** Here, we report the polymorphisms of 24 CYP enzymes using population-scale sequencing data, for 96 individuals of self-claimed healthy Malays and 105 Orang Asli. **RESULTS:** In total, there were 3264 genetic variants for the Malay population, comprising 2700 intronic and 564 exonic variants (Synonymous=65, Missense=100, 3'UTR=144, 5'UTR=12, Stop-gain=5, Splice region=15, Downstream=46, Upstream=21, Intergenic=152, Stop-lost=1, Splice acceptor=2, and Start-lost=1). For the Orang Asli, there were 3589 genetic variants; in which 2961 were intronic and 628 were exonic variants. Of the exonic variants, there were Synonymous=52, Missense=70, Frameshift=8, 3'UTR=215, 5'UTR=8, Stop-gain=2, Splice region=12, Downstream=57, Upstream=32, Intergenic=169, Stop-lost=1, and Splice acceptor=2. Overall, these two populations exhibit 126 low impact variants, 156 moderate impact variants, 26 high impact variants, and 5223 variants with modifier roles. The genetic variations confer either normal or extensive metabolism, poor metabolism or ultra-rapid metabolism of specific substrates. Carriers with poor metabolism status are predicted to have reduced capacity in biotransforming the respective substrates. This can result in drug accumulation, leading to adverse reactions or increased drug toxicity. Conversely, variants which confer rapid metabolizer status lead to the drug being cleared too quickly, potentially reducing its efficacy. **CONCLUSION:** Unraveling the distribution of different genetic variants in different populations is crucial for optimizing drug therapy and preventing potential adverse drug reactions in the respective populations.

Keywords: next-generation sequencing, pharmacogenomics, single nucleotide polymorphism.

POSTER PRESENTATIONS

P 01

IMPACT-CHD: THE USAGE OF RETROSPECTIVE POPULATIONAL DATA FOR MORTALITY PREDICTION MODEL

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INTRODUCTION: Coronary heart disease (CHD) continues to be Malaysia's leading cause of mortality despite better understanding of the disease and its management. Policymakers were challenged to improve populational health through effective treatment with limited resources. Assessing potential benefits to prevent death at a larger scale requires various considerations including population characteristics, disease prevalence and available treatments. Clinical trials are useful in treatment assessment but were unable to provide necessary evidence and generalisation. **METHODS:** A prediction model is an analytical method that considers events over time across population through the integration of values. A model such as IMPACT-CHD mortality model (IMPACT) permits the simulation of different scenarios within the population thus aids decision-making essential for policymakers. IMPACT utilizes MS EXCEL spreadsheet able to combine data from various resources to estimate death prevented or postponed (DPPs) over a specified time span. **RESULTS:** IMPACT allows the prediction of current mortality trends as well as future projections. In mortality trends of the particular retrospective populational data used, IMPACT was able to examine the consequences of risk factors and interventions on the DPPs. IMPACT proceeds to project the estimated proportion of 'life years gained' and 'cost effectiveness' through the alteration of treatment and risk factors. Due to its robustness, sensitivity and adaptability, IMPACT has been widely used internationally. The performance of IMPACT using Malaysian data have yet to be explored. **CONCLUSION:** Thus, utilising national primary and secondary data in developing the Malaysian -IMPACT-CHD model will be the next step to have better understanding of CHD in Malaysia.

Keywords: acute coronary syndrome, coronary heart disease, pharmacoepidemiology, prediction model, mortality

P 02
UNCOVERING THE CORRELATION BETWEEN CYP3A5*3 AND SLCO1B1*5 WITH STATIN-INDUCED MYOPATHY: AN EXPLORATORY STUDY AMONG A SOUTH-EAST ASIAN POPULATION

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INTRODUCTION: Although statins are generally well-tolerated, they are linked to musculoskeletal side effects known as statin-associated muscle symptoms (SAMS), which ranges from asymptomatic elevation to elevation of creatine kinase accompanied by muscle symptoms such as muscle pain and weakness. This caused a hindrance to statin adherence among patients, and hence predisposing them to cardiovascular event risks. Statin-associated muscle symptoms have been associated with single nucleotide polymorphism (SNP) in SLCO1B1 and CYP3A5 genes. In Malaysia, although statins are the predominant lipid-lowering drug prescribed, the genetic link between the SNP and statin adverse effects are yet to be established. This study aimed at determining the prevalence of SAMS, the prevalence of SLCO1B1*5 and CYP3A5*3 gene polymorphism, and to investigate the correlation between SLCO1B1*5 and CYP3A5*3 gene polymorphism with SAMS. **METHODS:** Subjects were recruited based on the inclusion and exclusion criteria. After obtaining ethics approval and patient consent, patients were interviewed for the occurrence of SAMS. Eligible patients had their blood withdrawn. Using a PCR-based method, SLCO1B1*5 and CYP3A5*3 gene polymorphism were detected. Genomic DNA extractions were performed using the NucleoSpin Blood Kit and the genetic polymorphism were detected using primers. Lastly, analysis and correlation of clinical data were performed using descriptive and inferential statistical analyses. **RESULTS:** While 52% of those of statins experienced SAMS, the SNPs were discovered in only 2% of the study population. The SLCO1B1 gene affected the expression of OATP1B1, which is a hepatic transporter of statin. Alternative allele 521T>C (SNP cluster ID rs4149056) gave rise to SLCO1B1*5 and the combination of 521T>C and 388A>G (SNP cluster ID rs2306283) gave rise to SLCO1B1*15 which were associated with decreased activity of OATP1B1. CYP3A5*5 was due to an alternative allele of 6986A>G (SNP cluster ID rs776746). **CONCLUSION**: Due to a dysfunctional metabolism mechanism associated with a non-functional CYP3A5 enzyme, this caused increased systemic exposure to statin and increased plasma concentration of statins which predispose such patients to greater statin adverse effects.

Keywords: statin-associated muscle symptoms, single nucleotide polymorphism

P 03

MOLECULAR DOCKING STUDY OF *POLYGONUM MINUS* EXTRACT (BIOKESUM®) AGAINST TROPOMYOSIN-RELATED KINASE B RECEPTOR (TRKB)

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INTRODUCTION: Brain-derived neurotrophic factor (BDNF) activates the tropomyosin-related kinase B (TrkB) receptor with high specificity and potency, regulating neuronal plasticity and survival in various central nervous system regions. Lower levels of BDNF and TrkB receptors are substantially related to neuronal death, resulting in cognitive impairment. Therefore, suggesting TrkB agonists might have therapeutic potential for neurodegenerative and neuropsychiatric disorders. *Polygonum minus* has been proven to have the ability to improve cognitive function. Thus, this study aims to identify compounds from *P. minus* extract (BioKesum®) that could act as agonists to the TrkB receptor, activating BDNF/TrkB signaling and enhancing cognition. **METHODS:** In this study, *in silico* screening was conducted on compounds from BioKesum® that were profiled through LC-MS analysis. A molecular docking approach was employed to evaluate the binding interaction of these compounds with the TrkB receptor. Seventeen (17) out of twenty (20) compounds from BioKesum® were filtered based on drug-likeness properties, and their binding interactions with the TrkB receptor were investigated. **RESULTS:** Among these compounds, taxifolin exhibited the lowest docking score (-6.35 kcal/mol), followed by glucocheirolin (-5.89 kcal/mol) and 4-p-coumaroylquinic acid (-4.25 kcal/mol). These compounds may contribute to the improvement of memory and cognitive function. **CONCLUSION:** The present findings suggest that the identified compounds in BioKesum® could serve as potential lead compounds in the treatment of cognitive dysfunctions and neurological illnesses caused by abnormal BDNF expression.

Keywords: BDNF, TrkB, *Polygonum minus*, cognition

P 04

EVOLUTIONARY GENOME MINING OF THE HUMAN ACE2 RECEPTOR AND SPIKE PROTEIN OF SARS-COV-2

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INTRODUCTION: COVID-19 is a threat to global health as it has infected millions of people with a wide spectrum of disease severity. Factors that contribute to this wide spectrum include age, underlying medical conditions and genetic makeup. Genetic factors are understudied with current available data often contradictory. This study aims to investigate the effect of reported polymorphisms of *ACE2* as well as mutations in different variants of the constantly evolving SARS-CoV-2 against COVID-19 severity. Mutations that alter protein structure could affect the binding affinity of the ACE2/SARS-CoV-2 interaction. An enhanced binding affinity could potentially increase the initial viral load and potentially cause severe disease. **METHODS:** Genome mining was done on in-house human genome database to extract available *ACE2* polymorphisms in the Orang Asli population. Orang Asli have lived in the Malay Peninsula for many years and are more exposed to environmental factors compared to the rest of the population. Additionally, they had inhabited the Malay Peninsular before migrations from other populations had occurred. Definitive mutations corresponding to different variants of SARS-CoV-2 were analyzed from the viral genomes downloaded from the GISAID database. **RESULTS:** Identified variants were selected based on their frequency and functional effect for homology modelling by SWISS-MODEL. The homology models were modeled based on 6 mutations in the Alpha-, 5 mutations in the Beta-, 5 mutations in the Delta-, 10 mutations in the Gamma-, 7 mutations in the Mu- and 17 mutations in the Omicron variants of SARS-CoV-2. **CONCLUSION:** By understanding the effects of these mutations on hosts with different *ACE2* genotypes, risk of COVID-19 severity could be predicted, and more efficient COVID-19 management and treatment approach can be strategized.

Keywords: *ACE2* polymorphism, COVID-19, genetic variation, genome mining, SARS-CoV-2, precision health

<u>P 05</u>
SOD2 GENETIC POLYMORPHISMS AND METHAMPHETAMINE-INDUCED PSYCHOSIS AND DEPENDENCE IN THE MALAYSIAN POPULATION

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INTRODUCTION: Methamphetamine (METH) is a highly addictive psychostimulant that has gained widespread popularity globally, including in Malaysia. Its addictive nature arises from its action on the central nervous system, leading to the release of neurotransmitters like dopamine, noradrenaline, and serotonin. Chronic METH use can result in dependence and potentially lead to METH psychosis. *SOD2* (superoxide dismutase 2) plays a crucial role in cell protection against damage caused by free radicals, which are implicated in METH-induced cell damage. Previous studies have associated the rs4880 (Ala/Val) polymorphism of the *SOD2* gene with the risk of developing METH psychosis. Therefore, this study aimed to investigate the association between *SOD2* genetic polymorphisms and METH dependence and METH-induced psychosis in a multi-ethnic Malaysian population. **METHODS:** Genotyping of four *SOD2* polymorphisms was performed in 246 METH-dependent subjects and 227 controls representing Malay, Chinese, Kadazan-Dusun, and Bajau ethnicities. **RESULTS:** Our findings showed that the rs2842980 polymorphism was significantly associated with METH dependence across all subjects. Stratification by ethnicity revealed significant differences in the Malay group for rs2842980 and rs2855116, in the Chinese and Kadazan-Dusun groups for rs4880 and rs2842980, and the Bajau group for rs2842980. Regarding METH-induced psychosis, rs4880 and rs2855116 exhibited significant associations specifically in the Bajau group. Furthermore, the T-T-A-T (rs4880-rs2758330-rs2842980-rs2855116) haplotype was significantly associated with METH dependence in all ethnic groups and pooled subjects. **CONCLUSION:** These findings suggest that these *SOD2* gene polymorphisms may contribute to the risk of developing METH dependence and METH-induced psychosis in the multi-ethnic Malaysian population. The study sheds light on the genetic factors influencing susceptibility to METH-related disorders and may have implications for personalized treatment approaches.

Keywords: methamphetamine, genetic polymorphism, *SOD2* gene, psychosis, Malaysian population

P 06

PERFLUOROOCTANOIC ACID (PFOA) EFFECTS TOWARDS WRL68 LIVER CELLS AND MCF7 BREAST CANCER CELLS PROLIFERATIONS

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INTRODUCTION: Perfluorooctanoic acid (PFOA) is a perfluorinated carboxylic acid that are widely used in industrial and commercial applications. But it has been detected in the environment, wildlife and humans. It is known to disturb the function of growth and sex hormones such as activating endocrine receptor (ER) and inducing ER-mediated transcription. **METHODS:** The cytotoxicity effects of different concentrations of PFOA ranging from 10 µM to 1000 µM on MCF7 breast cancer cells and WRL68 liver cells were investigated. **RESULTS:** In WRL68 cells, the cell viability started to decrease at the concentration of 500 µM. Meanwhile in MCF7, the cell viability spiked at 400 µM, with its peak at 600 µM. There is a possibility that PFOA interferes with the ER-positive MCF7 cells that caused them to increase in proliferation compared to WRL68. **CONCLUSION:** Further studies such as differential genes expression that are affected by PFOA in MCF7, and also MDA-MB-231 breast cancer cells that lacks ER should be performed to uncover the mechanisms involved.

Keywords: cytotoxicity assay, estrogen receptor, MCF7, perfluorooctanoic acid, WRL68

P 07
ADVANCING PRECISION HEALTHCARE: THE APPLICATION OF DNA WELLNESS SCREENING

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INTRODUCTION: The advancement of biotechnology in the post-genomics era has enabled the use of genetic tests to identify predispositions for a range of health conditions at an early stage in promoting proactive and personalized healthcare. Currently, there are more than 20 genetic test providers in Malaysia. The range of tests which are most commonly acquired by customers include prediction of disease risk, personality, nutrigenomics, sport-genomics, pharmacogenomics, and ancestry. **METHODS:** To achieve the aim of precision health which are prevention, prediction and personalized management, a comprehensive test that identifies all variations with known functions is required. In addition, a genotype-phenotype database that allows us to annotate the functional variants is a must to have. With the availability of these two fundamental keys, we have established a SNP array panel for direct-to-customer service. This service is made accessible to the people of Malaysia at an affordable cost. **RESULTS:** Our test consists of 10 panels comprised of ancestry (n=161 populations), allergy (n=14 traits), personality (n=32 traits), diet and nutrition (n=27 traits), obesity (n=49 traits), sport and exercise performance (n=23 traits), disease risk (n=187 traits), cancer (n=124 traits), Covid-19 risk (n=3 traits) and pharmacogenomics (n=123 traits). Customers were requested to send in samples either whole blood or buccal swab for the test. Good-quality DNA was isolated from whole blood and buccal swab samples with a success call rate of 99% for each sample analyzed using Asian Screening Array (ASA). The choice of sample type that is sent to us are influenced by factors such as the patient's age, medical condition, and test requirements as well as the customer preference. At the same time found that the factors that govern the choice of test providers include cost, availability of qualified consultants, after-test services and accuracy of tests and predictions. Besides, the readiness of the customers to know their genetic risks and assurance of data privacy are important considerations before getting the test done. **CONCLUSION:** As a start-up company, Zakesy Biotech takes into serious account the factors and needs of the customer and we offer affordable and high-quality genetic tests under the DNA Wellness Screening package. We also take the responsibility to provide awareness on the correct genetic testing concepts to reduce misunderstandings in this continuously evolving industry.

Keywords: SNP array, genetic testing, DNA wellness screening, personalized healthcare, industry.

P 08
THE IMPACT OF FOLIC ACID SUPPLEMENT ON HOMOCYSTEINE LEVELS IN CARDIOVASCULAR PATIENTS: A HOSPITAL-BASED STUDY

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INTRODUCTION: Homocysteine, an amino acid formed during the metabolism of the essential amino acid methionine, plays a role in energy metabolism and the production of neurotransmitters. Elevated homocysteine levels have been linked to cardiovascular disease. However, the association between high homocysteine and deficiency in folic acid is not well established. This study aimed to explore the interplay between folic acid supplementation, and homocysteine levels in a randomised 2 arm, placebo-controlled trial. **METHODS:** Patients were randomised to 2 groups; one group were given folic acid while another were given placebo. Liquid Chromatography-Mass Spectrometry (LCMS) was employed to quantify homocysteine levels. **RESULTS:** For the normal cardiovascular group, the average homocysteine concentration was 8.9 ± 2.71 µmol/l, while the intervention group exhibited a notably higher average concentration of 19.42 ± 4.00 µmol/l. Within the intervention group, prior treatment involving folic acid led to an average homocysteine concentration of 19.42 ± 4.00 µmol/l, which decreased significantly to 9.36 ± 3.98 µmol/l after supplementation. **CONCLUSION:** Based on current knowledge, it appears that elevated plasma homocysteine levels in cardiovascular patients can be mitigated through folic acid supplementation. However, it's worth noting that the initial treatment for these patients was aspirin, which has been associated with homocysteine level reduction in plasma. Despite the intended function of aspirin, some patients still exhibited elevated homocysteine levels. Further research is necessary to better understand these observed effects and potential contributing factors.

Keywords: Homocysteine, Cardiovascular disease, Folic acid, Aspirin

P 09

BETA-CARBOLINE COMPOUNDS AS POTENTIAL MULTI-TARGET ANTI-PROLIFERATIVE AGENT FOR BREAST CANCER

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INTRODUCTION: Current therapeutic agents for estrogen receptor (ER)-positive breast cancer are associated with adverse side effects and resistance. B-carbolines are natural indoles containing alkaloids that display a myriad of biological activities including anti-cancer, anti-inflammatory, anti-thrombotic, anti-bacterial, anti-fungal, anti-viral, and anti-leishmanial. Therefore, this study aims to identify the potential of beta-carboline derivatives as multi-targets anti-breast cancer agents against ER alpha (ERα), ER beta (ERβ), aromatase (AIs), and cyclooxygenase-2 (COX-2) using an *in-silico* approach. **METHODS:** A total of 55 beta-carboline compounds synthesized by the Institute of Science (IOS), UiTM were filtered for drug-likeness properties using QikProp. Molecular docking was performed to determine the binding of the 55 compounds that passed the drug-likeness criteria with four different targets which include ERα, ERβ, aromatase, and COX-2. **RESULTS:** From the docking analysis, there were five (5) compounds that exhibited good docking scores as ERα antagonists, ERβ agonists, AIs, and COX-2 inhibitors, respectively: (i) A1j (-7.618 kcal/mol, -8.300 kcal/mol, -4.446 kcal/mol, -6.561 kcal/mol); (ii) A1f (-7.454 kcal/mol, -8. 425 kcal/mol, -5.180 kcal/mol, -7.957 kcal/mol); (iii) A2a (-7.281 kcal/mol, -7.959 kcal/mol, -5.651 kcal/mol, -6.932 kcal/mol); (iv) A1m (-7.117 kcal/mol, -7.900 kcal/mol, -6.592 kcal/mol, -6.822 kcal/mol); (v) A1b (-6.829 kcal/mol, -7.499 kcal/mol, -4.461 kcal/mol, -7.281 kcal/mol). **CONCLUSION:** Based on these findings, the multimodal action of beta-carbolines offers opportunities for future drug development and optimisation against breast cancer.

Keywords: Beta-carbolines, ERα, ERβ, aromatase, COX-2, Ais

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A COMPARATIVE ANALYSIS OF COST EFFECTIVENESS AND USER FRIENDLINESS BETWEEN NANOPORE AND ILLUMINA TECHNOLOGIES IN COVID-19 SEQUENCING

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INTRODUCTION: The rapid evolution of sequencing technologies has revolutionized our ability to understand and combat infectious diseases like COVID-19. Illumina and Nanopore are two prominent sequencing platforms widely employed for this purpose. This study aims to compare the cost effectiveness and user friendliness of these technologies specifically in the context of COVID-19 sequencing. **METHODS:** Cost effectiveness analysis was conducted by assessing the expenses associated with sample preparation, sequencing, data analysis, and overall turnaround time. **RESULTS:** Illumina platforms often have a higher upfront cost to acquire the instrument, reagents, and specialized expertise in instrument operation. Therefore, the sequencing cost reaches RM604 per genome with a turnaround time of 7 working days. In contrast, Nanopore sequencers have a lower initial cost and require less complex sample preparation which costs RM75 to sequence one genome in 3 working days. Nanopore offers higher flexibilities in multiplexing the number of samples (12-96 samples per run) compared to Illumina (24 samples per run). Nanopore sequencing platform produces longer read length and lower number of coverages is required to yield 96-99% of the complete genome compared to Illumina (318-1189 vs. 598-3326 x coverage). **CONCLUSION:** Our analysis suggests that Nanopore sequencing holds a distinct advantage in terms of cost effectiveness and user friendliness for COVID-19 sequencing. Understanding the trade-offs between cost and user friendliness is crucial for the country to adopt a sustainable genomics-based surveillance programme for COVID-19 monitoring and research.

Keywords: COVID-19 sequencing, Illumina, Nanopore, cost effectiveness, user friendliness

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IN SILICO ANALYSES OF SYNTHESIZED CHALCONE, FLAVONE AND FLAVANONE AGAINST ESTROGEN RECEPTOR ALPHA AND BETA AS POTENTIAL THERAPEUTICS FOR BREAST CANCER

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INTRODUCTION: Breast cancer is the most common cancer in women worldwide. It is also the leading cause of cancer-related death in women with 14% mortality. Estrogen receptors are divided into two types; Estrogen Receptors Alpha (ERα) and Estrogen Receptors Beta (Erβ). ERα and ERβ work in contrary to each other, where ERα mediates cell proliferation and survivability and ERβ provides the inhibitory effects toward ERα. **METHODS:** In this study, 46 synthetic compounds derived from chalcone, flavone and flavanone were subjected to molecular docking to determine their interaction with ERα and ERβ. **RESULTS:** Based on the docking analysis, NP6, F3, NC2, NP7, NC7 showed the lowest binding energy of -8.03 < -8.01 < -7.93 < -7.92 < -7.88 kcal/mol, respectively against ERα (PDB ID: 3ERT). On the other hand, C20, F5, C18, NPc3, NP7 showed the lowest binding energy of –8.62 < -8.54 < -8.26 < -8.24 < -8.22 kcal/mol, respectively against ERβ (PDB ID: 5TOA). SwissADME analysis predicted that F3, NC2 and NC7 inhibit five (5) major CYP proteins, which could lead to toxicity due to substrate-enzyme inhibition. **CONCLUSION:** The search for more lead compounds with good docking properties and low toxicity continues as part of our research.

Keywords: Estrogen Receptor, Synthetic compound, Molecular Docking, AutoDock, SwissADME.