Third International Conference on Frontiers in Molecular Life Sciences

Multidisciplinary Research For Sustainable Development in the Post Genomic Era

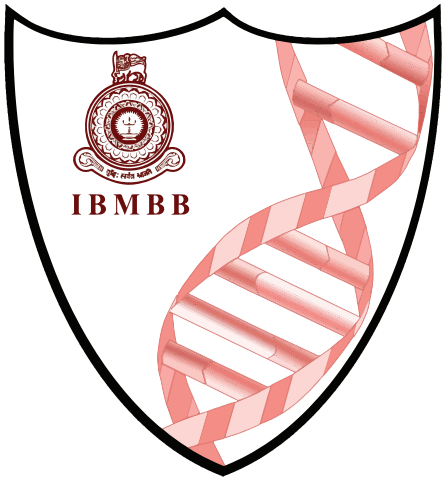
06th & 07th April 2022 — Colombo, Sri Lanka

PROGRAMME AND ABSTRACT BOOK

IBMBB

Third International Conference on Frontiers in Molecular Life Sciences

Institute of Biochemistry, Molecular Biology and Biotechnology - University of Colombo



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MESSAGE FROM THE DIRECTOR-IBMBB

On behalf of all the academics and students of the IBMBB, University of Colombo, I would like to extend our warmest welcome to all the delegates and participants for the 3rd International Conference on Frontiers in Molecular Life Sciences (ICFMLS), 2022 organized by IBMBB, University of Colombo.

This is one of the key events that facilitate interaction, sharing of knowledge, expertise, and experiences among academics and students. I am confident that ICFMLS 2022 will play an important role in addressing key issues of multidisciplinary research and developments in the country with a perspective of their practical deliveries. The broad scope of this event is to initiate an interactive platform to accommodate diverse activities in the field of Molecular Life Sciences.

The blend of symposia; from precision oncology to populational genetics and update on current COVID 19 pandemics to advance in immunotherapies, clearly indicates the diversity of the event and I'm confident that the two days conference proceedings give a very productive outcome for all our registered participants.

I would like to express my sincere gratitude to all the distinguished invited speakers for their presence and contribution to the conference. I also thank all the resource persons who have contributed in numerous ways to make this event successful.

Finally, I would like to keep a note of appreciation to the dedicated team at the IBMBB who worked tirelessly in bringing you a productive conference despite all the challenges during this difficult time.

Professor Prasanna Galhena
Director-IBMBB

MESSAGE FROM THE 3RD INTERNATIONAL CONFERENCE CO-CHAIRPERSONS

We are pleased to send this message to the 3rd International Conference on Frontiers in Molecular Life Sciences (ICFMLS) organized as a hybrid event to mark the 18th Anniversary of the Institute of Biochemistry, Molecular Biology and Biotechnology (IBMBB), University of Colombo. The theme of the 3rd ICFMLS held on 6th-7th April 2022 is "Multidisciplinary Research for Sustainable Development on Post-Genomic Era" which focus on the contribution of Molecular Life Sciences to sustainable development in Sri Lanka and also globally. This provides a forum for Sri Lankan students and scientists to gain cutting edge knowledge from renowned world authorities on a wide variety of topics including those that are highly pertinent in the current contexts.

We are extremely grateful for the support of Professor Pradeep Dharmadasa Acting Vice Chancellor, University of Colombo being the Guest of Honour. The keynote speaker for 3rd ICFMLS is Senior Professor Raj Somadeva, Professor of Archeology, Postgraduate Institute of Archeology, University of Kelaniya. This year, IBMBB is holding the International conference along with the events that are held annually. Thus we are having the Professor Stanley Wesner Memorial Lecture at the Inauguration of this conference. *Vidya jothi* Professor Vajira Dissanayake, Dean, Faculty of Medicine, University of Colombo who will deliver the Professor Stanley Wijesundera Memorial Lecture. There are seven symposia organized for the 3rd ICFMLS to cover themes ranging from Plant Metabolomics, Biotechnology, Population Genetics and Bioinformatics, Natural Products for therapeutics, Immunopathogenesis & Immunodiagnostics, Novel Vaccination & Drug Development Strategies and Molecular Genetics & Genomic Medicine. We are very grateful to the eminent speakers from Canada, India, Italy, Sri Lanka, United Kingdom and United States of America who will contribute to these symposia and share their knowledge with us to make this conference a success.

3rd ICFMLS will have 27 oral presentations and 21 poster presentations made by students and scientists from Sri Lanka (from the IBMBB and from other Higher Educational Institutes and from overseas. We are very pleased that this conference will provide a platform for the students and scientists to interact with eminent speakers to discuss the research findings.

On behalf of the IBMBB and the Organizing Committee, we thank Professor Pradeep Dharmadasa Acting Vice Chancellor, University of Colombo, family members of late Professor Stanley Wijesundera, the Keynote speaker, Stanley Wijesundera Memorial Lecturer, symposia speakers, chairpersons and judges for different Scientific Sessions, The oral and poster presenters, All our sponsors and all the members of the organizing committee. We sincerely hope that this conference will be intellectually stimulating to all the participants.

Professor Nimal Punyasiri
Co-Chairperson-ICFMLS 2022

Professor Shiroma Handunneti
Co-Chairperson-ICFMLS 2022

PROGRAMME

Day 1 – 6th April 2022		
	Room 1	**Room 2**
09.00 – 9.45 h	Inauguration ceremony	
9.45 – 10.45 h	**Prof. Stanley Wijesundera memorial lecture** **by** **Vidya Jyothi Prof. Vajira H. W. Dissanayake** Dean, Faculty of Medicine, University of Colombo.	
10.45 – 11.15 h	Tea break	
11.15 – 13.00 h	**Symposium I : Precision Oncology**	
13.00 – 13.45 h	Lunch +Industry talks	
13.45 – 15.00 h	**Oral Presentations - session 1** Natural products for therapeutics	**Oral Presentations - session 2** Immunopathogenesis & immunodiagnostics
15.00 – 16.45 h	**Symposium III** Trends in drug screening and development	**Symposium II** COVID-19 updates
16.45 – 17.15 h	Tea	
17.15 – 18.15 h	**Poster session 1**	

Day 2 – 7th April 2022		
	Room 1	**Room 2**
08.00 – 09.00 h	**Oral Presentation - session 3** Natural products for therapeutics	**Oral Presentation - session 4** Natural products for therapeutics
09.15 – 10.00 h	**Keynote address** **Prof. Raj Somadewa** Senior Professor of Archaeology Postgraduate Institute of Archaeology University of Kelaniya	
10.00 – 10.15 h	Tea break	
10.15 – 12.00 h	**Symposium IV** Peopling and evolution of languages **Oral Presentation - session 5** Population Genetics and Bioinformatics	**Symposium V** Natural products as immunity boosters
12.00 – 13.15 h	**Oral Presentation - session 6** Molecular genetics and genomic medicine	**Oral Presentation - session 7** Natural products for therapeutics
13.15 – 14.00 h	Lunch +Industry talks	
14.00 – 15.00 h	**Plenary lecture** **Prof. Eric Bongcam Rudloff** Professor of Bioinformatics Swedish University of Agricultural Sciences Uppsala, Sweden	
15.00 – 16.45 h	**Symposium VI** Plant genetic resources and Biotechnology	**Symposium VII** Trends and needs in immunodiagnostics and immunotherapeutics
16.45 – 17.00 h	Tea Break	
17. 00 –18.00 h	**Poster session 2**	
18. 00 –18.30 h	**Award ceremony and closing remarks**	

INVITED GUEST SPEAKERS AND SYMPOSIUM SPEAKERS

PROFESSOR STANLEY WIJESUNDERA MEMORIAL LECTURE

Vidya Jyothi Professor Vajira H. W. Dissanayake
Dean, Faculty of Medicine
Chair and Senior Professor
Department of Anatomy, Genetics and Biomedical Informatics
University of Colombo
Sri Lanka

KEYNOTE LECTURE

Professor Raj Somadewa
Senior Professor of Archaeology
Postgraduate Institute of Archaeology
University of Kelaniya
Sri Lanka

PLENARY LECTURE

Professor Eric Bongcam Rudloff
Professor of Bioinformatics
Department of Animal Breeding and Genetics
Swedish University of Agricultural Sciences
Uppsala
Sweden

SYMPOSIUM SPEAKERS

Dr. Kanishka De Silva
Consultant Oncological Surgeon
National Cancer Institute
Sri Lanka

Professor Rohan Siriwardana
Consultant Gastroenterological Surgeon
Faculty of Medicine
University Of Kelaniya
Sri Lanka

Dr. Janielle P. Maynard
Assistant Professor of Pathology and Oncology
The Johns Hopkins University
School of Medicine
USA

Dr. Chandima Jeewandara
Senior Lecturer
Department of Immunology and Molecular Medicine
University of Sri Jayewardenepura
Sri Lanka

Professor Shiroma Handunnetti
Professor of Immunology
Institute of Biochemistry, Molecular Biology and Biotechnology
University of Colombo
Sri Lanka

Professor Cheol-Hee Kim
College of Veterinary Medicine
Chumgnam National University
Daejeon
Republic of Korea

SYMPOSIUM SPEAKERS

Dr. Sirimal Premakumara

Senior Lecturer
Faculty of Nursing
University of Colombo
Sri Lanka

Dr. Asiri Galhena

Head-Research and
Development
Coke Atlanta
USA

Professor Sandagomi Coperahewa

Chair Professor
Department of Sinhala
University of Colombo
Sri Lanka

Professor Gyaneshwer Chaubey

Department of Zoology
Banaras Hindu University
(BHU) Varanasi
India

Professor Kamani Tennekoon

Prof of Molecular Life Sciences
Institute of Biochemistry, Molecular
Biology and Biotechnology
University of Colombo
Sri Lanka

Professor Priyani Pieris

Professor in Shalakya
Gampaha Wickramarachchi
University of Indigenous Medicine
Sri Lanka

Professor Ruckmani Kandasamy

Department of Pharmaceutical
Technology
Anna University
India

Associate Prof Melanie Coombs

Associate Professor in
Microbiology and Immunology
Acadia University
Canada

Professor Saman Seneweera

Faculty of Veterinary and
Agricultural Sciences
The University of Melbourne
Australia

Dr. Michela Troggio

Head - Crop Breeding
Research Group
Fondazione Edmund
Mach
San Michele all'adige
Italy

Professor Ajith Karunarathne

Associate Professor and Chair of
Graduate Examinations
University of Toledo
OH USA

Professor Prasanna Galhena

Director
Institute of Biochemistry, Molecular
Biology and Biotechnology
University of Colombo
Sri Lanka

Dr. Rajiva de Silva

Consultant Immunologist
Head Department of Immunology
Medical Research Institute
Sri Lanka

Professor Sugandhika Suresh

Professor in Biochemistry
Faculty of Medical Sciences
University of Sri Jayewardenepura
Sri Lanka

ORAL PRESENTATIONS

OP 01: Melatonin and Serotonin activity among long-term, skilled meditators
Thambyrajah JC, Handunnetti SM, Dilanthi HW, Dissanayake DWN

OP 02: Comparison of immunoreactive proteins profile of pathogenic and non-pathogenic serovars of *Leptospira*
Anuradha WGK, Gangani PD, Fernando N, Karunanayake L, Tammitiyagodage MG, Handunnetti SM

OP 03: Evaluation of SARS-CoV-2 Specific Antibodies in Sri Lankan Patients: A Preliminary Study Using an In-house ELISA
Pathirana SL, Gunasekara P, Premawansa G, Namalie D, Fernando N, Perera IC, Nanayakkara S, Kumarasinghe D , Gangani PD, Thambyarajah J, Deepachandi B, Perera T, Siriwardana S, Manilgama S, Sumathipala S Muthugala R, Rajapakse S, Dassanayake D, De Silva R, Handunnetti S, Premawansa S, Nitsche A

OP 04: A preliminary study on mitochondrial D-loop variations in sporadic breast cancer patients of Sri Lankan Tamil, Sri Lankan Moor and Sinhalese populations
Kotelawala JT, Tennekoon KH, Ranasinghe R, Rodrigo HACIK, De Silva GKS, PereraWAHA, Yoganathan N, Manatunga MRS, Dissanayake DMAS, Joseph N, Rajasooriyar C, Indranath K

OP 05: Role of Kiss1/ Kisspeptin/ GPR54 system in the development of polycystic ovary syndrome (PCOS) in Sri Lankan women
Umayal B, Wijesundera WSS, Chandrasekharan NV, Wijeyaratne CN

OP 06: Prevalence of *PNPLA3* polymorphisms in a cohort of non-alcoholic steatohepatitis (NASH)-related hepatocellular carcinoma (HCC) patients in Sri Lanka
Samarasinghe SASM, Hewage AS, Siriwardana RC, Tennekoon KH, Niriella MA, De Silva S

OP 07: Molecular surveillance of Artemisinin-resistant k13 mutations in imported *Plasmodium falciparum* cases diagnosed in Sri Lanka
Gunasekera WMKT deAW, Weerasena OVDSJ, Handunnetti SM, Premawansa S, Premaratne RG, Fernando SD

OP 08: Detection of hotspot regions of *WT1* gene in a cohort of 46,XY DSD children in Sri Lanka
Arambage MK, Hewage S, De Silva S, Atapattu N, de Silva KSH

OP 09: Maternal genetic affinities of Sri Lankan pre-historic and modern populations with the populations in the Eastern world and Australia
Fernando AS, Ranasinghe R, Tennekoon KH, Karunanayake E, Somadeva R, Rai N

OP 10: Mitogenome diversity in Sinhalese and indigenous Vedda population in Sri Lanka
Welikala AHJ, Ranasinghe R, Tennekoon KH

OP 11: Selective anti-breast cancer activity of endophytic fungi isolated from *Rhyzophora apiculate*
Wickramaratne NS, Thusyanthan J, Bandara CJ, Ranasinghe R Karunaratne DN, Tennekoon KH, Samarakoon SR

OP 12: Selective cytotoxicity of marine macroalgae extracts on oral cancer cells (UPCI:SCC 090 and UPCI:SCC 152)
Kumarasamy S, Piyathilaka MAPC, Samarakoon SR, Tennekoon, KH, Ranasinghe R

OP 13: Acetylcholinesterase inhibitory activities of *Jasminum multiflorum, Jasminum rottlerianum, Darcena sanderiana and Sansevieria zeylanica*
De Silva WS, Wijayarathna CD and De Silva HIC

OP 14: Determination of anti-tubercular activity of selected phytochemicals using molecular docking
` Liyanage S, Perera O, Mudalige H

OP 15: Protein-ligand docking for the identification of ligand binding sites and novel therapeutics for breast cancer
Saleem T, Perera O, Mudalige H

OP 16: Isolation of an anti-cancer compound from *Mangifera zeylanica* leaves and investigation of potential cytotoxic effects
Perera AADN, Samarakoon SR, Ediriweera MK, Tennekoon KH

OP 17: Protein-ligand docking of phytochemicals against Alzheimer's disease
Jafar J, Perera O, Mudalige H

OP 18: Preliminary study on phytochemical analysis and GC-MS fingerprints of Sri Lankan traditional polyherbal drug "Panu"
Lakshman GVCP, Madhushanka LWN, Rasangani AWP, Wageesha NDA

OP 19: Virtual Screening and Molecular Dynamics Based Identification of Bismahanine as a Potential Anti-Aging Compou Withdrawn
Mishal MFM, Senathilake KS, Samarakoon SR

OP 20: In silico Identification and In Vitro Validation of Alpha Hederin as a Wnt/β catenin pathway inhibitor in b Withdrawn **m cells**
Peter ST, Mishal MFM, Senathilake KS, Samarakoon SR

OP 21: Antibacterial properties in "*Madhuca longifolia*" leaves and seeds extractions against selected Gram negative and positive microbial strains.
Vitharana TA, Bandaranayake U

OP 22: Effect of a polyherbal formulation in Sri Lankan market on the mRNA expression and secretory levels of inflammatory cytokines in THP-1 derived human macrophages
Ranaweera BVLR, Abeysekera AM, Weerasena OVDSJ, Handunnetti SM

OP 23: Immunostimulatory effect of a polyherbal formulation in the Sri Lankan market: Enhancement of IgG expression levels
Ranaweera BVLR, Abeysekera AM, Weerasena OVDSJ, Handunnetti SM

OP 24: Cytotoxicity of *Allophylus cobbe* extracts against human hepatocellular carcinoma (HepG2) cells
Thusyanthan J, Wickramaratne NS, Senathilake KS, Samarakoon SR, Tennekoon KH, Thabrew MI

OP 25: Effect of *Vernonia zeylanica* on non-IgE mediated degranulation and histamine release by RBL-2H3 cells in vitro
Kulathunge SSB, Rukshala BAD, Premawansa WS, Handunnetti SM, Pathirana PPSL

OP 26: *In-vitro* Anti-inflammatory Properties of the Ethyl Acetate Soluble Proanthocyanidins (EASPA) from the Immature Inflorescence of *Cocos nucifera* L.
Tenne PCRK, Peiris LDC, Abeysekera A, Padumadasa S, Dissanayake DMAB, Galhena PB, Padumadasa C

OP 27: Effectiveness of *Aegle marmelos* (Bael) fruit and leaf extracts against selected *Candida* species
Wanigasekara DN, Wickramasinghe SS, Wijeratne WMDGB, Napagoda MT

OP 28: Identification of potential therapeutic agents for COVID-19 through site-specific protein-ligand docking
Nadarajah N, Perera, O, Mudalige, H

OP 29: Protein-ligand docking study to identify ligand binding sites against Hepatitis B protein receptor
Rizwan R, Perera O, Mudalige H

POSTER PRESENTATIONS

PP 01: In-house Development of a Rapid Antigen Test for Detection of SARS-CoV-2 Infections
Pathirana SL, Gunasekara P, Deepachandi B, Janage SN, de Silva R, Dassanayake D, Fernando N, Weerasena J, Handunnetti S

PP 02: Elevated cytokine gene expression levels in patients with psoriasis
Abbasbhoy FS, Rajapakse S, Akarawita J, Gunasekara C, Fernando P, Ranaweera L, Pathirana S, Handunetti S, Fernando N

PP 03: Cross-reactivity of sera of patients allergic to venom of Sri Lankan ant species with *Apis dorsata* and *Vespa affinis* venom
Peiris TMR, Gunasekara P, Handunnetti SM, Dasanayake D, De Silva R

PP 04: Assessment of A10398G polymorphism in the *MT-ND3* gene in sporadic breast cancer patients of Sinhalese ethnicity
Jayasekera BMLP, Ranasinghe R, Kotelawala JT, Senathilake KS, De Silva K, Tennekoon KHT

PP 05: Genomic surveillance of SARS-CoV-2 virus among infected people in Sri Lanka
Perera T, Uddin S, Gunasekara P, Brinkmann A, Premawansa G, Namalie D, Siriwardana S, Ku CS, Periaswamy B, Dasanayake D, Manilgama S, De Silva R, Fernando N, Gangani PD, Thambyarajah J, Rajapakse S, Sumathipala S, Muthugala R, Kohl C, Handunnetti S, Premawansa S, Perera IC, Pathirana S, Nitsche A

PP 06: Association of selected genetic variants in *CBS* gene with clinicopathological characteristics in a cohort of children with Homocystinuria in Sri Lanka
Samarasinghe MHNJ, De Silva S, Punyasiri N, Jasinge E

PP 07: Association of selected genetic variants in the *MTHFR* gene and clinicopathological characteristics in a cohort of children with homocystinuria in Sri Lanka
Mahaliyanage DT, De Silva S, Punyasiri N, Jasinge E

PP 08: Verification of the presence of mesenchymal stem cells in primary human endometrial cell
Tenne PCRK, Galhena PB, Dissanayake DMAB, Padumadasa S, Harikrishnan JD, George GDN, Peiris LDC, Abeysekera A, Padumadasa C

PP 09: Analysis on the structural genomic rearrangements in major cancers
Withdrawn
Jayathunga WH, Weerakoon WRW, [illegible], Wangchuk P, Singh G

PP 10: Characterisation of complete *GH1* gene deletions discerned in two children with isolated growth hormone deficiency
Nuha FN, Sundralingam T, Hewage AS, de Silva KSH, Tennekoon KH

PP 11: Isolation and molecular identification of some selected fungi with lignin degradation activity.
Siriwardana RSGTN, Weerasena OVDSJ, Gunaratna LNR

PP 12: Genome-wide analysis of *GATA* gene family in angiosperms
Withdrawn
Rajapaksha RLPND, Kathriarachchi HS, Wanasuriya AM

PP 13: Effect of *Exobasidium vexans* infection in tea (*Camellia sinensis.* (L.) O. Kuntze) on the expression of flavonoid biosynthetic enzymes and biosynthesis of flavonoids
Edirisinghe KAMJ, Gunaratna LNR, Nimal Punyasiri PA, Weerasena OVDSJ

PP 14: Development of DNA based accurate identification method for agarwood produced by endemic threatened *Gyrinops walla*
Lewke Bandara N, Priyankan S

PP 15: Comparison of rat immune responses to two pathogenic *Leptospira* serovars prevalent in Sri Lanka
Gangani PD, Anuradha WGK, Fernando N, Karunanayake L , Rajapakse S, Premawansa, S Handunnetti SM

PP 16: Effect of aqueous extracts of cinnamon bark on hyperglycaemia in diabetes induced Wistar rat models
Wijenyaka GMUD, Bulugahapitiya VP, Jayasinghe SS

PP 17: Protein-ligand site-specific docking for Plasmepsin-II Malaria receptor and identification of ligands and their binding sites
Fernando F, Perera O, Mudalige H

PP 18: Protein-ligand docking for the identification of therapeutic ligands against the Nipah virus attachment glycoprotein using AutoDock
Ekneligoda T, Perera O, Mudalige H

PP 19: Scientific investigation on Sri Lankan polyherbal drug ''Neelagiri Padmana'' for its antioxidant activity, polyphenol content and GC-MS analysis
Madhushanka LWN, Lakshman GVCP, Ratnayake RMCG, Ariyawansha HA, Wageesha NDA

PP 20: A molecular docking study revealed natural benzophenones and xanthones from *Garcinia zeylanica* as Wnt and Hedgehog pathway inhibitors in breast cancer stem cells
Rajagopalan U, Samarakoon SR, Saliu TP, Tennekoon KH, Senathilake K, de Silva ED

PP 21: Effect of *Munronia pinnata* on function of DENV-3 and interaction of DENV3 and endothelial cells
Munezero PC, Handunnetti SM, Fernando NTRG, Ranaweera LR, and Hapuarachchi SD

PP 22: Phytochemicals Coated Silver Nanoparticles as Potential Vehicles for the Delivery of Plant Natural Products
Kalansuriya P, Lokunarangoda AJ

PP 23: Antioxidant, antibacterial, and antifungal activities of flowers of *Hibiscus spp*
Rajapaksha RMK, Edirisinghe EMRKB

Professor Stanley Wijesundera Memorial Lecture

Genetics and Genomics in the Sri Lankan population - Insights from Four Decades of Service and Research

Vidya Jyothi Professor Vajira H. W. Dissanayake MBBS, PhD, FNASSL, FIAHSI

Dean, Faculty of Medicine
Chair and Senior Professor, Department of Anatomy, Genetics and Biomedical Informatics
University of Colombo
Sri Lanka
Chairperson - Global Genomic Medicine Collaborative (G2MC)
vajira@anat.cmb.ac.lk

Genetics and genomics play a vital role in clinical practice today. Genetics refers to the study of genes and the way that certain traits or conditions are passed down from one generation to another. Genomics describes the study of all the genes of a person (the genome). Over time genetic and genomic technologies have advanced from tests that enabled testing of chromosomes (in the 1960s), to tests that enabled testing individual genetic variants (in the 1980s), to tests that enable testing of chromosomes for microdeletions and duplications, and to tests that enable testing of genes, gene panels, exomes and genomes (today). As such now it is possible not only to establish the genetic aetiology of conditions of which the phenotype clearly indicates a well-known monogenic disorder through single gene testing but also the genetic aetiology of conditions where the phenotype is not clear but there is a suspicion of an underlying genetic aetiology through gene panel, exome or genome testing. In addition advances in the understanding of genetic variants as predictors of treatment outcomes have enabled the use of such knowledge in treatment decision making and prognostication. Furthermore advances in the understanding of the role of genetic variants in absorption, metabolism, excretion and distribution of drugs (pharmacogenomics) have made it possible to use such knowledge in treatment decision making.

The Human Genetics Unit in the Faculty of Medicine, University of Colombo established in 1983 has been in the forefront of genetic and genomic research in the country for four decades. The Unit conducts service and research using cytogenetic, molecular genetic, and molecular cytogenetic techniques. This work has enabled us to catalog the spectrum of cytogenetic abnormalities and microdeletion syndromes in children; the genetic aetiology of a range of conditions including Duchenne Muscular Dystrophy, Spinocerebeller Ataxia, Huntington Disease, Tuberous Sclerosis, Hereditary Haemochromatosis, and Hereditary Thrombophilia to name a few; and the diversity of pharmacogenomic variants in the Sri Lankan population and to compare it with other global populations.

The advent of the genomic medicine era saw the Human Genetics Unit taking leadership in sequencing a Sri Lankan genome and implementing genomic medicine technologies to diagnose Inherited Cancer Syndromes and Undiagnosed Rare Genetic Disorders. Up to date the Unit has sequenced and analysed over 500 exomes. This work has led to the discovery of a range of novel variants contributing to the aetiology of these conditions.

Several large-scale research projects conducted by the Unit resulted in new discoveries. Among this work is the pioneering discovery of the contribution of variants in the EGF gene to the aetiology of pre-eclampsia and the weight of babies at birth; the description of the microbiome of the placenta in a subset of women with pre-eclampsia; conclusively showing that Y-chromosome microdeletions do not contribute to recurrent pregnancy loss, and discovery of the contribution of several genetic variants in the aetiology and the pathophysiology of sporadic breast cancer in post menopausal women.

The work described above has enabled the Human Genetics Unit to become one of the leading centres for genetic and genomic service and research among Low and Middle Income Countries (LMICs) and the orator being appointed as Chairperson of the Global Genomic Medicine Collaborative an organisation dedicated to advancing genomic medicine in LMICs established by the participants of the Meeting of the Global Leaders in Genomic Medicine convened by the National Genome Research Institute of USA in Washington, DC, USA in January 2014.

In this oration I shall describe in detail the work mentioned above.

Keynote Lecture

KEYNOTE LECTURE

Archaeology meets Genomics: new avenues of population prehistory

Professor Raj Somadeva

Postgraduate Institute of Archaeology
University of Kelaniya
Sri Lanka

Dispersal patterns of ancient languages have been considered as a strong indicator of prehistoric population distribution all over the world. Archaeological evidence provides parallel clues as complementary to elaborate the relationship held between linguistic dispersal and population diversity. Such diffusions occurred in a time which was far beyond the past when before the written records emerged such diffusions occurred in a time which was far beyond the past when before the written records emerged and therefore narratives are absent about the prehistoric linguistic interactions held. Most of the histories belonging to the diverse nations in the world have memories of such immigrations. Memories of migrations related to their ancestral populations appear in different forms. The stories pertaining to the peopling of Sri Lanka are also enmeshed by such a story that is strongly rooted in the public consciousness of identity. The arrival of a gang who had a north Indian cultural origin and their subjugation of the native then being inhabited the island by them is the major content of that story. The idea of population migration associated with mainland India brings us a sound theme to be analyzed scientifically. Any attempt to be focused on the study of the composition of the prehistoric population in Sri Lanka has to scrutinize the population dynamics in South Asia from a broad base of biological point of view. Perhaps it might be spatially incorporated further into mainland Southeast Asia. Analysis of the complexity of the composition of the lingua franca in mainland India is an important point of departure to formulate a conceptual framework on the biological inheritance of the prehistoric population in Sri Lanka. On one hand, the language family of Indo-Aryan derived from the Central Asian wave of linguistic influence that occurred 3.5ka ago dominated in most part of the northern part of mainland India even including Pakistan and Bangladesh. On the other hand, South Indian Peninsula was dominated by Dravidian languages. This was a result of a high level of endogamy triggered by the strict social boundaries and a high degree of genetic drift encouraged by long-term isolation. The investigations carried out using mitogenome analysis of autosomal data and Y-chromosome lineages on the population history for mainland India suggest that the maternal lineages emerged 55-65ky ago and a major population shift triggered in the late Pleistocene. Linguistic information provides a beacon to resolve the problems relate to those characteristics. The inspirations of the rises and falls of such dynamics might shed a light on determining some of the dilemmas posited on the genetic inheritance of the prehistoric population by the recent archaeological findings in Sri Lanka.

keyword: Sri Lanka, population history, archaeology, south Asia

Plenary Lecture

PLENARY LECTURE

From Precision Agriculture to Personalised Medicine: A wholistic view of future and present research in the Life Science

Professor Eric Bongcam Rudloff

Professor of Bioinformatics
Department of Animal Breeding and Genetics
Swedish University of Agricultural Sciences
Uppsala
Sweden

For the past several decades, agricultural technology has made tremendous progress in new technologies that leads to increased crop yields and more efficient use of inputs such as water and fertilizer. An increased and more efficient production of food is needed for the world population that is Expected to Reach 10 billion by 2050. Precision agriculture and food production technologies go hand to hand and face new challenges.

The phrase 'You Are What You Eat' means that it is important to eat proper food to be healthy and fit. More and more evidence suggests that there is a connection between the microbiome, the host genome, food intake and health. One issue that will be discussed during my presentation is the problem concerning the development of diseases in animals and humans due to effects of the preservation and the processing of food. Another topic will discuss the impact that processed food has on the microbiome.

Scientific research produces more and more complex data to address the above-mentioned issues. My talk will mention some of the trends in Artificial Intelligence dealing with those multidisciplinary based studies.

SYMPOSIUM ON PRECISION ONCOLOGY

Invited lecture 1

Management of cancers in Post Genomic era : Answers we got and Questions that remains

Dr. Kanishka De Silva

Consultant Oncological Surgeon
National Cancer Institute
Sri Lanka

Cancer is a heterogeneous disease with different risk factors , clinical outcomes and treatment responses. Most cancers are due to acquired risk factors leading to lifetime non inherited mutations. About 10-20% are due to inherited germline mutations. Interestingly same mutational carriers can get different cancers and benign conditions, but yet others survive a normal life still carrying the same genes. The interactions between inherited and environmental factors lead to progressive accumulation of genetic and epigenetic changes in cells that ultimately ends up as dysplasia and invasive cancers.

The knowledge of genes, gene products, cell signaling pathway receptors and other molecules associated with development of cancer has provided us with a better understanding of the disease. This has created a new window to screen at risk families in primary prevention, modify surgical strategies in treating affected individuals, develop targeted treatment strategies, predict therapeutic responses as well as prognostication.

The knowledge of epigenetic phenomenon such as DNA methylation, Histone deacetylation etc.leading to development of cancer or blocking it, is essentially still incomplete. These alterater gene expressions such as inactivation of several DNA repair genes including BRCA1, ATM, CHK2, and P53. The end result is a sporadic cancer with a biological behavior similar to the phenotypes produced by inherited mutant carriers such as BRCA1. These abnormalities are potentially reversible by inhibitors of DNA methylation and histone deacetylation. This knowledge can be used to treat relevant subsets of sporadic cancer patients as well as screen detected mutational carriers to preventive their genes getting expressed in their lifetime.

Today we know that DNA is not our destiny, although it plays a huge role in shaping it. Genetics loads weapons, but it is epigenetics that pulls the trigger.

SYMPOSIUM ON PRECISION ONCOLOGY

Invited lecture 2

NAFLD induced Hepatocellular carcinoma – unique disease in Sri Lanka

Professor Rohan Siriwardana

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Hepatocellular carcinoma (HCC) is a disease with a grave prognosis. Worldwide, it is related to infective hepatitis. However the pattern of disease is predicted to change with the change in aetiology of chronic liver cell disease. In the near future Non Alcoholic Fatty Liver Disease (NAFLD) will be the leading cause for chronic liver cell disease globally. Sri Lanka has one of the highest incidences of NAFLD in the world. NAFLD has already become the leading case for liver cirrhosis in Sri Lanka. As a result, the pattern of HCC that we see in Sri Lanka is what is expected to see globally in the near future. HCC is commonly seen in non-cirrhotics and morphology is different in our patients. There are many diagnostic and therapeutic challenges faced in these patients due to late presentation. Detecting HCC early by screening high risk groups is a strategy to overcome these challenges.

SYMPOSIUM ON PRECISION ONCOLOGY

Invited lecture 3

P2X4 Purinergic Receptors as a Therapeutic Target in Aggressive Prostate Cancer

Dr. Janielle P. Maynard

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USA

Prostate cancer (PCa) remains a leading cause of cancer-related deaths among men and treatment options for metastatic PCa are limited. There is a critical need to identify new mechanisms that contribute to PCa progression, that distinguish benign from lethal disease, and that have potential for therapeutic targeting. P2X4 belongs to the P2 purinergic receptor family that is commonly upregulated in cancer and is associated with poorer outcomes. We observed P2X4 protein expression primarily in epithelial cells of the prostate and on a subset of immune cells. Our analysis of patient prostate cancer tissues representing 491 PCa cases demonstrated significantly elevated P2X4 expression in cancer compared to benign tissue, in precursor lesions, and in cases with common genetic alterations. High P2X4 expression in benign tissues was likewise associated with the development of metastasis after radical prostatectomy. Treatment with P2X4-specific agonist CTP increased transwell migration and invasion of PCa cells. P2X4 antagonist 5-BDBD treatment resulted in a dose-dependent decrease in cell viability and decreased cell migration and invasion. Knockdown of P2X4 attenuated growth, migration, and invasion of PCa cells. Finally, knockdown of P2X4 in mouse PCa cells resulted in significantly attenuated subcutaneous allograft growth. Collectively, these data strongly support a role for the P2X4 purinergic receptor in PCa aggressiveness and identifies P2X4 as a candidate for therapeutic targeting.

SYMPOSIUM ON COVID-19 UPDATES

Invited Lecture 1

Once told: Virus is “Simply a piece of bad news wrapped up in protein."

Dr. Chandima Jeewandara

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Department of Immunology and Molecular Medicine
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Sri Lanka

The dawn of 2020 was a turning point in our modern era and global health. We have learned a hard lesson about the intrinsic vulnerability of our societies to a single pathogen. Metagenomic sequencing allowed the scientists the ability for early sharing of SARS-CoV-2 genome sequences and allowed health authorities to develop countermeasures to prepare the world for the COVID 19 pandemic.

Revealing the sequences significantly contributes to public health decisions during the current COVID-19 pandemic or future outbreaks, especially with the emerging variants of the SARS-CoV-2 virus.

Identifying the causative agent for COVID 19 pandemic and its global spread was only possible through virus genome sequencing. Additionally, virus genome sequences are fundamental in investigating outbreaks, designing diagnostic assays, drugs, and vaccines. Analysis of SARS-CoV-2 virus genomes helped to complement, augment and support strategies to reduce the burden of COVID-19.

My talk will summarize our work at the Allergy Immunology and Cell Biology Unit (AICBU) of the University of Sri Jayewardenepura on the SARS-CoV-2 sequencing from isolates collected throughout the different phases of the pandemic to determine the molecular epidemiology of SARS-CoV-2 in Sri Lanka. I will be highlighting the evolution of the SARS-CoV-2 virus, including the current circulation of viruses with mutations that may confer greater transmissibility and threaten the efficacy of vaccines in Sri Lanka.

The longer the virus circulates, the more opportunities for it to mutate. Coordinated sequencing of virus genomes can help evaluate the possible new risks associated with new mutations of the SARS-CoV-2 virus. However, the lack of effective coordinated efforts in genomic sequencing is one of the key highlights we observe in Sri Lanka as the pandemic continues to unfold.

SYMPOSIUM ON COVID-19 UPDATES

Invited Lecture 2

Immunopathogensis of COVID-19: *What We Should Know*

Professor Shiroma Handunnetti

Professor of Immunology
Institute of Biochemistry, Molecular Biology and Biotechnology
University of Colombo
Sri Lanka

The Coronavirus Disease-2019 (COVID-19) which is caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) had imposed public health emergency and affected millions of people around the globe. As of March 2022, over 470 million confirmed cases of COVID-19 along with more than 6 million deaths were reported worldwide. SARS-CoV-2 infection causes excessive production of pro-inflammatory cytokines which leads to the development of “Cytokine Storm Syndrome.” This condition results in uncontrollable inflammation that further imposes multipleorgan-failure eventually leading to death. SARS-CoV-2 induces uncontrolled innate immune response and impairs adaptive immune responses thereby causing tissue damage. Thus, understanding the most prominent features and evolution of innate and adaptive immunity to SARS-CoV-2 is crucial in understanding COVID-19 outcomes as well as in developing effective strategies to control COVID-19. The sequential key immunological events that occur during SARS-CoV-2 infection and are involved in the immunopathogenesis of COVID-19 will be discussed. This will also highlight some of the therapeutic options already in use such as immunosuppressive drugs, plasma therapy and intravenous immunoglobulins along with various novel potent therapeutic options that should be considered in managing COVID-19 infection such as traditional medicines and probiotics.

SYMPOSIUM ON TRENDS IN DRUG SCREENING AND DEVELOPMENT

Invited Lecture 1

Functional validation of candidate genes for mental disorders using zebrafish

Professor Cheol-Hee Kim

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Daejeon
Korea

The zebrafish has become an appropriate animal model in the analysis of numerous human diseases. Given the translational relevance of zebrafish, multidisciplinary studies employing behavioral, neurobiological, and molecular methods with this species may provide insights into human mental disorders. Recently, genome-wide association studies (GWAS) have provided candidate genes for a variety of mental disorders, several of which are known to be comorbid with abnormal social behavior. In order to investigate and validate GWAS candidate genes, we have taken a systematic, targeted knockout (KO) approach to establish various disease models in zebrafish. To date, we have validated the function of human candidate genes involved in Kallmann syndrome, Potocki-Shaffer-syndrome, Miles-Carpenter syndrome, Down syndrome/autism, and Armfield syndrome. Recently, we have also established targeted KO zebrafish for clinically important genes involved in autism spectrum disorders, X-linked intellectual disability, childhood ataxia with CNS hypomyelination, congenital hypothyroidism, attention deficit hyperactivity disorder, schizophrenia, and bipolar disorders. In addition, our zebrafish center also maintains zebrafish KO lines involved in emotional control, e.g. anxiety or aggression, and movement disorders, such as infantile spasm/epilepsy and amyotrophic lateral sclerosis. For phenotypic analysis, we have established and utilize a battery of social interaction tests including shoaling, group behavior, mirror biting, alarm substance, body size preference, color preference, and a three-chamber social choice task. From bench to bedside, our efforts have made contributions to the recently established international patient foundations, ZC4H2 Deficiency Research Foundation and DeSanto-Shinawi Syndrome Foundation. In closing, the Zebrafish Center for Disease Modeling (ZCDM) is trying to contribute to the zebrafish research community for the advancement of technical methods and application of zebrafish KO lines related to human disease.

SYMPOSIUM ON TRENDS IN DRUG SCREENING AND DEVELOPMENT

Invited Lecture 2

Drug discovery from Marine Natural Products – Current status and future trends

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According to the latest review of Newman & Cragg (2020), of the drugs approved within the last four decades, 1418 (75.4%) were with natural products origins. Only 463 drugs are of pure synthetic origin. Although most drugs are still derived from terrestrial sources, a considerable number of drugs, drug candidates and other interesting highly divers metabolites are reporting from marine sources. About 30,000 compounds of marine origin are reported to date and more than 1,000 compounds are newly discovered each year. They are often characterized by structural novelty, complexity, diversity, biological activities and potency in comparison to its terrestrial counterparts. From the oldest known marine natural product Tyrian purple from marine molluscs by the Phoenicians around 1600 BC and marine biopolymers like agar and carrageenan, the vitamins A and D or polyunsaturated fatty acids like EPA and DHA, there are many drugs of marine origin in the western pharmacopeia in the recent years. The real marine drug development started with the discovery of spongothymidine and spongouridine in the 1950s from the Caribbean sponge *Tethya crypta*. Then the antibiotic, Cephalosporin C, produced by the fungus *Acremonium chrysogenum* isolated in the 1940s, was the starting point for the development of the antibiotic class of cephalosporins. When look at patents on marine natural products, it reveals a strong increase since middle of 1980s and most compounds isolated are from marine invertebrates. Marine natural products research in Sri Lanka was mainly done collaboratively at the Colombo University and were on metabolites from algae, slugs, sponges and soft corals reported with interesting compounds with potent bioactivities and some of which had gone to clinical level studies.

The Bioprospecting on marine natural products in pharmacological point of view at present, is mainly on cytotoxic and cytostatic drugs. Consequently, the anti-cancer compounds represent more than half of the new marine natural products discovered from 1985, followed by anti-bacterial compounds. The trend in bioprospecting is that the marine environment will remain a promising source of natural products, molecules, and drugs of therapeutic use. Therefore, drugs from marine sources will have a promising effect on several chronic and challenging diseases in the years to come.

SYMPOSIUM ON TRENDS IN DRUG SCREENING AND DEVELOPMENT

Invited Lecture 3

Principles of Liquid Chromatography-Mass Spectrometry: Driver in drug discovery and screening

Dr. Asiri Galhena

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USA

Drug discovery and screening is a labor-intensive and time-consuming process that comes with a significantly high price tag. Recent advancement in Mass Spectrometry (MS) has evolved to the point where it is used throughout this process and plays a crucial role. In particular, when MS is coupled with a chromatographic separation technology, it becomes a powerful analytical tool, which adds an orthogonal detection function for the sample analysis. MS is based on the generation of gas-phase analyte ions, the separation of these ions according to their mass-to-charge ratio (m/z), and the detection of these ions. The introduction of electrospray ionization (ESI) has enabled the MS analysis of highly polar molecules, ranging from small molecules to large biomacromolecules, a critical element in the drug discovery workflow. However, there is a foundational knowledge gap in the drug discovery research community when it comes to MS-based method development. This short presentation provides a general introduction to LC-MS, mainly from a functional point of view. Next to the basic understanding of operating principles of ionization techniques, mass analyzers, and method development.

Invited Lecture 1

Revisiting the Origin and Evolution of the Sinhala Language

Professor Sandagomi Coperahewa

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Sri Lanka

Languages, like human beings, belong to families based on their genetic relationships. Sinhala, the language spoken by the Sinhalese, is a member of the Indo-Aryan family of languages. Opinions about the origin of the Sinhala language are also related to the origin of the Sinhala ethnic group. It was only at the beginning of the last century that scholars began to focus on the evolution of the Sinhala language. The debates focused on the Indo-Aryan linguistic affinities in Sinhala and non-Indo-Aryan (Dravidian) relations. A key point discussed among the scholars who recognized Sinhala as an Indo-Aryan language was from which part of India the first groups who settled in Lanka came to this island. Not only linguistic factors but also genealogical narratives, geographical locations, and ethnic relations were important in these debates. The dominant legend about the origin of the Sinhala language and the ethnic group was the story of Vijaya in the chronicles. It has also been suggested that Sinhala or *Hela* is a locally inherited language. The stock of *Nispanna* words in the Sinhala language is not related to other Indian languages. The linguistic features of Sinhala show the composite character of the language. Linguistic and genetic affinities can provide new insights into the origin and evolution of the Sinhala language. Through a review of the opinions expressed on the origin and evolution of the Sinhala language, this lecture emphasizes revisiting the linguistic and genetic affinities that exist between the different ethnic groups of Sri Lanka.

*Keywords***:** Sinhala; Sinhalese; Indo Aryan; Dravidian; linguistic affinities

Invited Lecture 2

The spectrum of migrations in and out of India in the last two millennia

Professor Gyaneshwer Chaubey

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Varanasi
India

The existence of Siddi, Jews, and Parsi communities in India and Roma in Europe has been noted since ancient times. However, due to the lack of high-resolution genetic data, their origin and affiliation with other Indian and non-Indian populations remain shrouded in legends. Previous genetic studies on Indian Jews populations have found evidence for a minor shared ancestry of Indian Jews with Middle Eastern (Jews) populations. In contrast, the Iranian link was proposed for Parsis. Similarly, The Siddi, who Portuguese rulers have brought, and Roma, who has left India in the last 1500 years, has not been tested well on molecular data. However, these studies had relied on fewer individuals and haven't studied the detailed admixture process of Indian Siddi, Jews, Parsis, and Roma with the local Indian populations. Here in a large sample size using a combination of high resolution biparental and uniparental markers (Y chromosome and mitochondrial DNA), we reconstruct a broad genetic profile of Indian Siddi, Jews, Parsis, and Roma, focusing on the effects of cultural practices on patterns of genetic diversity.

SYMPOSIUM ON TRENDS IN PEOPLING AND EVOLUTION OF LANGUAGE

Invited Lecture 3

History meets Genetics

Professor Kamani Tennekoon

Senior Professor of Molecular Life Sciences
Institute of Biochemistry, Molecular Biology and Biotechnology
Sri Lanka

Sri Lanka appears to have been populated by humans approximately 125,000 years before present (YBP), but skeletal evidence for Anatomically Modern Humans dates back to only about 38,000 YBP. Mitochondrial DNA (mtDNA) exclusively inherited maternally helps us to decipher our maternal lineage. In Sri Lanka, majority of the mtDNA haplogroups seen among contemporary ethnic populations belong to the M Macrohaplogroup whereas the majority of mtDNA haplogroups in Adivasi (Vedda) clans belong to the N Macrohaplogroup. When phylogeography of haplogroups are examined while majority have a South Asian (Indian) affiliation, a considerable presence (20 to 25%) of West Eurasian haplogroups are seen among Sinhalese, Sri Lankan Tamils and Adivasi clans. Besides, Eastern, South East Asian and Pacific haplogroups have also been identified among Sri Lankans, albeit at a very low frequency. Migration of people between Sri Lanka and India is well documented in historical chronicles. Though of a lesser degree, movement of people between South East Asia and Sri Lanka and East Asia and Sri Lanka are also recorded. There does not seem to be a record of a major movement of women directly to Sri Lanka from West Eurasia. Considerable presence of West Eurasian mitochondrial haplogroups among Adivasi clans who are considered to descend from early inhabitants, and among Sinhalese and Sri Lankan Tamils, two contemporary ethnic populations with a longer history in the island, tempts us to speculate some of them being descendants of those arriving through the beachcomber route during dispersal of AMH out of Africa directly or via the Indian subcontinent.

Invited Lecture 1

Ayurvedic concepts on immunity

Professor Priyani Pieris

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Immunity is a biological term that describes a state of having sufficient biological defences to avoid infections, disease or other unwanted biological invasion. In Ayurveda Medical Science, the concept of immunity is described under the heading of *Vyadhikshamatva*. The word "*Vyadhikshamatva*" means the factors which limits the pathogenesis and opposes the strength of a disease. It has two sub types, "*Vyadhi – balavirodhitva"* which is the capacity or strength to resist the progress of disease and "*Vyadhi – utpadakapratibandhakatva"* is the resisting power of the body to prevent the occurrence and reoccurrence of the disease. There are nine factors mentioned in Ayurveda which are responsible for decreasing the immunity.

According to Ayurveda medical Science, a person is called healthy or "*Swastha*" if possesses an equilibrium state of the *dosa* (body humors), *Agni* (bio -digestive fire), *Dhatu* (tissues) and *Mala* (waste products of body) associated with a pleasant state of soul, sensory organs and mind. It is the basis for normal immunity. Due to unwholesome food, regime and drugs disequilibrium or derangement of *Dosa* etc. causes diseases.

Ojas is the supreme essence of *Saptadhatu* (seven bodily tissues) which appeared foremost in the human body during embryogenesis. And it is the seat for biological strength hence called *Bala*. It is of three types, *Sahaja* (genetic) inborn resistance to disease, *Kalaja* (temporal) strength which achieved based on the division of seasons and the age of the person and *Yuktikrita* (acquired) is the one which is induced with the help of dietary and other regimens influences to increase the *Vyadhikshamatva.*

The concept of immunity and immunomodulation are extensively explored and used in Ayurveda medical science particularly in the form of *Rasayana* therapy. Rasayana improves nutritional status and better qualities of *Dhatu* and strengthening the *Ojas (Bala*) and leads to attributes longevity, *Vyadhikshamatva* (immunity against diseases), improved mental and intellectual competence.

Invited Lecture 2

Phyto based Natural products as Potential Therapeutics

Professor Ruckmani Kandasamy

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Department of Pharmaceutical Technology
Anna University
India

Natural products and their structural analogues have historically made a major contribution to treatment of diseases due to its value-added therapeutic constituents. In the present scenario developed countries are marching towards the utilization of traditional medicinal systems involving herbal drugs as indicated by the World Health Organization. However, due to the reduced efficacy, lack of scientific justification, standardization challenges, development of herbal medicine is becoming a challenging task. Novel targeted drug delivery technology may increase the efficacy and reduce the side effects of various phyto compounds. With this basic idea recently herbal medicines are developed in to novel phyto based formulations. The pressing need is to integrate novel drug delivery system and plant medicines to combat various diseases. Phytoconstituents generally possess an inherent drawback of limited oral bioavailability and instability owing to their hydrophilic nature. Due to lack of scientific justification and processing difficulties, including standardization, mostly herbal medicines were not considered for development as novel formulations. However, modern phytopharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required etc.) of herbal medicines to be incorporated in novel drug delivery system, such as phytosomes, topical gels, hydrogels, nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles etc. Few companies are focusing towards the development of phyto based therapeutic products such as nano curcumin, *Ginkgo biloba* phytosomes, *Camellia sinesis* phytosomes, Panax ginseng phytosome etc. My lecture will focus on novel approaches towards the development of phyto based drug delivery systems with recent technologies involved in the development of phytosomes and phyto based gels. Special emphasis will be made towards the startup companies focusing towards phyto based works and about the facilities available with us for collaboration towards the development of novel phyto based drug delivery products.

Invited Lecture 3

Natural products for boosting immunity against infectious diseases

Associate Professor Melanie Coombs

Associate Professor in Microbiology and Immunology,
Acadia University
Canada

Flavonoids are polyphenolic phytochemicals made in plants. These polyphenols have many different bioactive functions including immune modulatory and anti-microbial activity. There is evidence suggesting that flavonoids improve patient recovery from infections such as pneumonia. Depending on the flavonoid and context, phytochemicals may promote or inhibit immune cell function. Therefore, given the increasing use of flavonoids as nutraceuticals, there is a need to clarify the role of flavonoids in the modulation of human immune responses. Here we review and highlight key ways that flavonoids boost immune responses. Flavonoids improve responses to pathogens often by reducing inflammation. Some flavonoids make epigenetic modifications of NF-κB-regulated inflammatory expressed genes in the Toll-like receptor (TLR)-4 signaling pathway, contributing to their immune modulatory activity. Many cancer chemotherapies are immunosuppressive leaving patients vulnerable to infections. Flavonoids such as myricetin and apigenin enhance innate and adaptive immune responses and may be useful immunomodulatory agents in patient populations with impaired immune responses. Nutraceuticals may improve response to pathogens by decreasing mediators of inflammation while increasing T cell and NK cell activity. Our understanding is improving concerning the impact of flavonoids on diverse biological processes. Flavonoids impact immune responses to pathogens and the consumption of flavonoid-rich fruits and vegetables may improve overall immune function in humans. Better understanding the mechanism of action of flavonoids in humans needs to be further studied.

Invited Lecture 1

Biofortification of cereal with zinc: Opportunities to improve zinc loading into the grain

Professor Saman Seneweera

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The University of Melbourne
Australia

Zinc (Zn) is an essential micronutrient for all life forms, including humans. It is estimated that approximately two billion people are deficient in zinc. Human dietary zinc intake is primarily derived from cereals, predominantly rice (*Oriza sativa* L) and wheat (*Triticum vulgare* L). The concentration of Zn in both cereals is very low, owing primarily to yield enhancement breeding and climate change. Following the Green Revolution, consistent breeding efforts helped to increase yield potential and disease resistance, but grain quality aspects such as micronutrients in grain were largely ignored. On the other hand, climate change, especially rising CO_2 levels, lowers the grain Zn concentration because of changes in the plant's primary and secondary metabolism. This also lowers other grain quality attributes such as protein and iron (Fe).

Biofortification has been identified as the most effective way to address global zinc malnutrition. However, this is still a very difficult task because there is limited understanding on the molecular processes that control Zn uptake, transport, and grain loading, which are all important for Zn biofortification of cereals.

In this presentation, the magnitude of zinc deficiency and zinc-associated nutritional disorders are discussed in global context. The main factors that contributed to lower grain Zn levels in cereals are discussed in detail, with a focus on plant genetic and environmental interactions. Furthermore, key molecular and physiological processes of Zn uptake, transport, and grain loading are elaborated, while major limitations for biofortification are identified. In our research, Zn loading into the grain and its distribution within the grain have been identified as a major bottleneck for Zn biofortification. This analysis was further supported by physiology, genomic, proteomic, and Synchrotron X-ray fluorescence analysis. Anatomical barriers in the vascular region at the base of the grain, as well as physiological and molecular constraints in the crease region, are recognized as other key limitations for Zn biofortification. Further, it has been identified that Zn movement from the endosperm cavity into the modified aleurone layer is then regulated by the ZIP and YSL transporter systems. Overall, these findings suggest that grain Zn concentration can be increased through target breeding and genetic engineering to address global Zn malnutrition.

Invited Lecture 2

Genomic and genetic tools for breeding in fruit trees

Dr. Michela Troggio

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San Michele all'Adige (TN)
Italy

With the advent of next generation sequencing and the significant reductions in sequencing costs the technology has brought about de-novo assembly of complex genomes, and re-sequencing of multiple genotypes within a species have become feasible. The availability of reference genomes for many plant species is causing a rapid acceleration in genetics and genomics research by providing new tools to identify genes and other functional elements, as well as a more efficient development of improved varieties. Understanding the links between phenotypic variation and their underlying DNA variation is one of the major challenges for plant geneticists. High-density SNP arrays for genome-wide assays of allelic variation, and highly parallel sequencing, have now made high resolution genetic characterization of crop germplasm feasible paving the way towards genomics-assisted breeding.

Invited Lecture 1

A glimpse at compartmentalized subcellular signaling

Professor Ajith Karunarathne

Associate Professor and Chair of Graduate Examinations
University of Toledo
OH, USA

Despite their uber complexity, contemporary cellular sciences still examine the regulation of cellular responses such as growth, invasion, and apoptosis primarily upon global pharmacological or genetic perturbations. However, little is known about how cells respond to asymmetric external stimuli that unevenly activate cell surface receptors; how the resultant signals propagate into the 3D cell interior, explore specific organelles; and controls effectors. We engineer optogenetic signaling actuators with precise spatial and temporal signaling acuity and interrogate how distinct subcellular domains of cells communicate upon localized signaling control. Our results show that coordinated molecular communications between cell compartments deliver pharmacologically crucial cellular outputs.

Invited Lecture 2

Targeting cellular signaling in Cancer; Opportunities, challenges and limitations

Professor Prasanna Galhena

Director
Institute of Biochemistry, Molecular Biology and Biotechnology,
University of Colombo
Sri Lanka.

Tumour biology is a highly complex, rapidly evolving series of mechanisms which focus on cell survival, proliferation, metastasis, and resisting to therapies. Heterogenicities associated with these mechanisms give rise to an existence of phenotypically and functionally distinct cell populations within the tumor microenvironment that are either promote the tumourgenesis or actively involved in proliferation, perhaps promoted by surrounding normal stromal and inflammatory cells.

Cellular signaling mediates through several molecular pathways is now identified as one of the major drives in tumour pathophysiology and immensely contributing to the observed tumour heterogenicity. In the era of targeted therapies, substantial efforts are being made to interfere with these signaling pathways, yielding a mixed clinical outcome. With the emergence of novel tools in molecular testing, there is an exponential growth in the field of personalized cancer care at an extremely high cost for the patient over a compromised treatment outcome, thus debating their use in the current practice. Most of these genetic tests are not either initiated by healthcare providers, or clinically validated and mostly driven by the industry, thus raising dilemma for their actual clinical outcome.

Therefore, it is a timely requirement to revisit the current concept of “Consumer Genomics” with the objectives of enhancing its clinical validity by optimizing test protocols, assuring test outcomes, and test regulation by autonomous accreditation bodies.

Invited Lecture 3

Novel immunotherapeutics

Dr Rajiva de Silva
Consultant Immunologist
Head Department of Immunology
Medical Research Institute
Sri Lanka

Immunotherapy is the treatment of a disease with therapeutic agents that promote or inhibit immune responses. Newer agents are also being developed. They include monoclonal antibodies, recombinant cytokines and cellular therapy. This presentation looks at some of the therapies developed in cancer (CAR T cell therapy, immune check point inhibitors), allergies (oral immunotherapy for food allergy) and SARS – CoV – 2 infections.

RESEARCH PAPERS - ORAL PRESENTATIONS

OP 01 (Abstract # 5)

Melatonin and serotonin activity among skilled long-term meditators

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Melatonin and its precursor serotonin are neurotransmitters that play an important role in the physiological regulation of mood, sleep, and behaviour. Studies have shown changes in the levels of melatonin and serotonin following meditation. However, the outcome of Buddhist meditation on both these neurotransmitters collectively have not been studied. Therefore, the objective of this study was to assess melatonin and serotonin activity in long-term, skilled meditators and to compare them with an age, gender, and education level matched, non-meditating group. Long-term, skilled meditators (n=18) were recruited using a validated interview. The serum melatonin and serotonin levels of long-term, skilled meditators and age gender and educational level matched control subjects (n=18) who had never practiced meditation, were determined using commercial ELISA kits (LDN, Nordhorn, Germany). Melatonin and serotonin activities of the meditators and controls were compared using Mann-Whitney U test for non-parametrically distributed data. The mean age of the meditator group was 42.77 ± 9.51 and the control group was 42.54 ± 10.43 years, and 67% were males. The mean duration of the meditation practice was 6.46 ± 2.89 years. In the meditator group, the melatonin (18.5 ± 0.62 pg/ml) (Mean ± SEM) and serotonin activity (140.2 ± 3.79 ng/ml) were significantly higher compared to the control group [melatonin (16.9 ± 1.31 pg/ml; p=0.025) and serotonin (122.6 ± 4.19 ng/ml; p=0.002)]. The finding of significantly elevated melatonin and serotonin activity in the skilled long-term meditators compared to the non-meditator control subjects suggest that Buddhist meditation is potentially beneficial in decreasing stress and in improving relaxation in individuals.

Keywords: meditation, melatonin, serotonin, neurotransmitters, stress

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OP 02 (Abstract # 41)

Comparison of immunoreactive proteins profile of pathogenic and non-pathogenic serovars of *Leptospira*

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Leptospirosis is an emerging fatal illness leading to an estimated decrease of 2.9 million disability-adjusted life years (DALYs) worldwide each year. The majority of leptospiral infections are asymptomatic, or the symptoms may mimic those of several other unrelated infections, making clinical identification challenging. Identification of the most appropriate *Leptospira* antigens potent in inducing immune responses in pathogenic and non-pathogenic serovars is the initial step of the process in developing an antigen detecting diagnostic test. This study aimed to compare the immunogenic antigen profiles of the most prevalent pathogenic serovars/serogroups of *Leptospira* and one non-pathogenic serovar of *L. biflexa*. Antigen preparations were made from whole-cell lysates of serovars/serogroups; Australis, Bangkinang, Pyrogenes, Hebdomadis, and Patoc by sonication and characterized using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (10% gels). Rabbit immune serum was raised against these five different serovars, following four intravenous immunizations with *Leptospira* antigens on the 01, 08, 15, and 28 days. Both homologous and heterologous hyperimmune rabbit sera were used to determine the immunoreactive antigens in the non-pathogenic and the different pathogenic serovars of *Leptospira*. Twenty-three antigen bands having molecular weights of 11- 142 kDa were observed as shared major proteins in the four pathogenic and the non-pathogenic serovar (Patoc). Immunoblotting with hyperimmune rabbit sera detected that the circulating serovars/serogroups of *Leptospira* in Sri Lanka have certain commonly expressed immunoreactive protein profiles. Eight and two antigens (ranging from Mw 32-111 kDa) from serovar Patoc, Bangkinang, Australis, Hebdomedis and Pyrogenes were detected being immunoreactive with rabbit IgG and IgM respectively. The four tested pathogenic and the non-pathogenic serovars/serogroups demonstrated similarities in their protein profiles. Further characterization of shared antigens will be important to determine the cross-reactivity among the *Leptospira* serovars/serogroups and for the development of immunodiagnostics based on antigens conserved between serovars.

Key words: *Leptospira*, immunoreactivity, serovars, immunization and cross-reactivity

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OP 03 (Abstract # 51)

Evaluation of SARS-CoV-2 specific antibodies in Sri Lankan patients:a preliminary study using an in-house ELISA

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In the absence of successful antiviral drugs, the anti-SARS-CoV-2 antibodies developed either by vaccination or natural infection play a major role in mounting protection against SARS CoV-2 infection. The aim of this study was to assess anti-SARS CoV-2 antibodies in individuals infected with SARS-CoV-2, using in-house IgM and IgG enzyme-linked immunosorbent assays (ELISA) in order to validate it against a commercially available ELISA kit (EuroImmune). Total IgG and IgM levels in sera (n=50) of laboratory confirmed SARS-CoV-2 patients from North Colombo Teaching Hospital were evaluated and compared with sera (n=50) collected from healthy individuals (pre-pandemic) as controls. Sample collection was initiated before the vaccination programme was rolled out in Sri Lanka. However, about 3/18 patients had their first dose of vaccine before sample collection. Seropositivity of 90.0% (n=45/50) was observed for both IgG and IgM anti-SARS-CoV-2 antibodies in confirmed cases, while none of the controls were seropositive. Seropositivity of confirmed cases with either IgM or IgG was 94.0% (n=47/50). In contrast, the seropositivity of only 76.0% (n=38/50) was demonstrated with commercial ELISA kits for the detection of IgG or IgM. All samples detected seropositive by commercially available kits remained seropositive with either in-house IgM or IgG ELISAs. Most patients (>80.0%) were seropositive, regardless of age (<60 years vs >60 years), gender (male vs female) or clinical severity (mild vs moderate/severe). Most seropositive patients (92.9%, n=39/42) either by IgG or IgM ELISA had clinical symptoms for 1-4 weeks while only 7.1% (n=3/42) were seropositive in those who had ≤ 1 week of clinical symptoms. This is the first report on evaluation of anti-SARS-CoV-2 antibodies using an in-house ELISA in Sri Lankan patients. These data suggest that the two in-house ELISAs developed are suitable to assess anti-SARS-CoV-2 antibody levels induced by either natural infections or vaccination.

Key words: SARS-CoV-2, seroprevalence, ELISA, in-house assay

Acknowledgements: This work was supported by IDEA project, Robert Koch Institute (RKI), Germany.

OP 04 (Abstract # 15)

A preliminary study on mitochondrial D-loop variations in sporadic breast cancer patients of Sri Lankan Tamil, Sri Lankan Moor and Sinhalese populations

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In Sri Lanka, breast cancer remains the most prevalent cancer diagnosed in women. Approximately 90-95% of breast cancer incidents are estimated to be 'sporadic' in occurrence. Early diagnosis, through biomarkers, can have a positive impact on disease prognosis. Mitochondrial DNA has been studied for its potential use as a biomarker in predicting disease, metastasis and drug response. However, mitochondrial DNA also show population-specific variations. This study reports mitochondrial DNA D-loop variations in sporadic breast cancer patients of Sri Lankan Tamil and Sri Lankan Moor ethnicities compared with previously published data on the Sinhalese ethnicity.
Patients of Sri Lankan Tamil (n=35) and Sri Lankan Moor (n=31) ethnicities were enrolled in this study. Individuals of Sri Lankan Tamil (n=30) and Sri Lankan Moor ethnicities (n=30) from a prior study, who were generally regarded as healthy, were analysed as the control group. The mitochondrial D-loop region was amplified using PCR and DNA sequencing was performed through Sanger sequencing. Sequence data was compared to the rCRS reference sequence. Fischer's exact test was used to compare the prevalence of variants between patients and respective controls. The variations 73G, 263G, 315insC were observed in nearly all individuals. Variations such as 146C (p=0.02), 489C (p=0.033), 16223T (p=0.0004) were shown to be significantly associated with patients of Sri Lankan Tamil ethnicity; while 480C (p=0.007) was associated with patients of Sri Lankan Moor ethnicity. However, none of the above
variations showed significant associations with either patients or controls of Sinhalese ethnicity. Variations at 16223 have been previously reported in cancer. In addition, 489C and 16223T have shown to impact mitochondrial transcription of respiration complexes in studies conducted on cybrids, indicating a possible role in mitochondrial/metabolic dysfunction which is implicated in pathogenesis of cancer. Suitability of these variants aspredictive biomarkers for specific populations need to be further explored.

Keywords: mitochondrial DNA; breast cancer; Sinhalese; Sri Lankan Tamil; Sri Lankan Moor

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OP 05 (Abstract # 46)

Role of Kiss1/ Kisspeptin/ GPR54 system in the development of polycystic ovary syndrome (PCOS) in Sri Lankan women

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Polycystic ovary syndrome (PCOS) is a highly prevalent endocrine disorder in women of reproductive age. Its complex pathogenesis involves a disturbance in the hypothalamic-pituitary-gonadal axis. The menstrual cycle is controlled by the hypothalamic GnRH pulse generator, pituitary gonadotropes, ovaries and uterus; of which, the GnRH pulse generator is most important. Kisspeptin, produced by the Kiss1 gene, binds to GPR54 receptors on GnRH neurons, stimulating the release of GnRH hormone; which stimulates the secretion of LH and FSH, providing the hormonal trigger for the menstrual cycle. Since GnRH secretion is dysregulated in PCOS, it can be postulated that altered patterns in the Kiss1/kisspeptin/GPR54 system may play a role in the development of PCOS. This study aimed to identify the role of Kiss1/Kisspeptin/GPR54 in the development of PCOS. Women with PCOS symptoms from adolescence (n=55) and adult controls (n=110) were recruited. Serum kisspeptin levels were determined by ELISA. Whole gene sequencing was performed to identify the polymorphisms in Kiss1 and GPR54 genes. Crude odds ratios and a 95% confidence interval were used to assess the magnitude of risk factors in the development of PCOS. Serum kisspeptin concentrations were significantly higher in PCOS subjects (cases vs. controls - kisspeptin 4.87 *vs.* 4.13 nmol/L; $p<0.05$). Serum kisspeptin was positively associated with PCOS (OR=1.85; 95%CI-1.25–2.76; p=0.002). Sequencing of GPR54 gene revealed 5 SNPs-rs10407968, rs1250729403, rs350131, chr19:918686 and chr19:918735 with the latter two being novel polymorphisms. Sequencing of Kiss1 gene revealed 2 SNPs-rs5780218 and rs4889. Serum kisspeptin levels can be used as an early marker of PCOS to identify the condition post-puberty. Genetic variations in GPR54 and Kiss1 genes are unlikely to be associated with PCOS in Sri Lankan women. Heterozygous allele of chr19:918686 of GPR54 gene may be associated with serum kisspeptin concentrations, suggesting a potential role in the aetiology of PCOS.

Keywords: PCOS, Kisspeptin, Kiss1, GPR54

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OP 06 (Abstract # 47)

Prevalence of *PNPLA3* polymorphisms in a cohort of non-alcoholic steatohepatitis (NASH)-related hepatocellular carcinoma (HCC) patients in Sri Lanka

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Hepatocellular carcinoma (HCC) is a primary liver cancer ranking as the sixth most common cancer worldwide. “Non-alcoholic steatohepatitis” (NASH) has become a major risk factor for HCC as most of the recent cases of HCC in humans appear to arise in the absence of advance fibrosis or cirrhosis. Apart from dietary factors, variants in the key genes of lipid metabolism can predispose individuals to NASH- associated HCC. Three single nucleotide polymorphisms (SNP) in the *PNPLA3* (Patatin-like phospholipase domain-containing 3) gene have been linked with the presence of NASH-associated liver pathogenicity in different populations. The objective of the current study was to analyze the genetic background of NASH-related HCC with respect to three common *PNPLA3* gene variants (rs738409, rs2281135 and rs2294918) in a Sri Lankan NASH-related HCC patient cohort. A cross sectional study was carried out on a group of forty-eight NASH-related HCC patients. Primer extension-based SNP analysis was used to genotype all three polymorphisms in the study cohort. The most common genotypes and alleles were CG (79%) and C (60.4%) for the rs738409 polymorphism, GG (66.66%) and G (68.75%) for the rs2281135 polymorphism and GG (64.58%) and G (77%) for the rs2294918 polymorphism respectively. The present study describes the prevalence of *PNPLA3* gene polymorphisms with regard to the genetic background of NASH-related HCC in a Sri Lankan patient cohort for the first time. The prevalence of the risk alleles were within the range of allele frequencies reported in other populations. Furthermore, a case-control study is also in progress to compare these findings with healthy controls and cirrhosis controls without HCC.

Keywords: hepatocellular carcinoma, non-alcoholic steatohepatitis, single nucleotide polymorphisms, *PNPLA3*, Sri Lanka

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OP 07 (Abstract # 49)

Molecular surveillance of Artemisinin-resistant k13 mutations in imported *Plasmodium falciparum* cases diagnosed in Sri Lanka

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Artemisinin-based combination therapy (ACT) is the drug of choice for treatment of uncomplicated *Plasmodium falciparum* malaria. The emergence of artemisinin partial resistance has led to delayed parasite clearance (day-3 parasitaemia). If the partner drug is resistant, this will result in treatment failure. The importance of molecular surveillance of artemisinin-resistance has been highlighted by a strong correlation between point mutations in the Kelch protein propeller domain (k13) and delayed parasite clearance following treatment with ACT. This study determined the molecular epidemiology of k13 genotypes in imported *Plasmodium falciparum* patients diagnosed in Sri Lanka during the phase of prevention of re-establishment of malaria. Patients diagnosed with *Plasmodium falciparum* between April 2014 and December 2019 were included. Parasite isolates extracted from pre -treatment samples were analyzed for polymorphisms in k13-propeller domain, and parasitaemia on the third day was monitored. A 849 base pair fragment in the Kelch protein propeller domain in chromosome 13 (PF3D7_1343700) was amplified by a nested PCR, followed by purification and direct sequencing using ABI BigDye Terminator v3.1 cycle sequencing kit and an ABI 3730 sequencer (Applied Biosystems, USA). An electropherogram was generated, and sequences were analyzed using BioEdit software. Consensus sequences were compared with the reference 3D7 isolate (PF3D7_134700) to locate point mutations. Nine synonymous mutations and one non-synonymous mutation were detected among the 72 samples that were successfully sequenced. The non-synonymous mutation R561H detected in this study is a validated marker of artemisinin partial resistance. The patient had travelled to Rwanda, a country where the R561H mutation is highly prevalent. Initial parasitaemia was 249 parasites/µL. Parasitaemia persisted for 3 days, confirming artemisinin partial resistance. This is the first report highlighting the risk of k13 mutations entering Sri Lanka through travel routes, while emphasizing the importance of molecular surveillance to control the spread of drug-resistant malaria in Sri Lanka.

Key words: malaria, *Plasmodium falciparum,* artemisinin resistance, k-13 mutations

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OP 08 (Abstract # 58)

Detection of hotspot regions of *WT1* gene in a cohort of 46,XY DSD children in Sri Lanka

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Disorders of Sex Development (DSD) are explained as a discordance between a person"s genetic sex and phenotypic sex. Thus, an infant with a karyotype of 46,XY and ambiguous genitalia will have a 46,XY DSD. Wilms" tumor suppressor gene 1 (*WT1*) codes for Wilms" tumor protein 1, a transcriptional regulator that is involved in sex determination and development of the urogenital system. *WT1* mutations in male patients with a DSD could result in Wilms" tumor, which accounts for 90% of total paediatric renal cancers. Several syndromes including Denys Drash Syndrome, Frasier Syndrome, Nephrotic Syndrome type 4 and WAGR syndrome (Wilms" tumor, Aniridia, Genitourinary anomalies, mental Retardation) are also associated with *WT1* mutations. The objective of this study was to determine the hotspot mutations in the *WT1* gene in a cohort of 46,XY DSD children in Sri Lanka. Children (N=7) with a 46,XY karyotype and ambiguous genitalia, aged 2 weeks to 10 years were selected for the study. DNA was extracted from patients" blood samples and exon 9, intron 9 and exon 10 of the *WT1* gene were screened for variants, using sequence-specific primers and sanger bi- directional sequencing. Pathogenic variant c.1399C>T, p.Arg467Trp (rs121907900) was detected in one patient, and benign intronic variant c.1265-32C>A (rs2232593) was detected in three patients. Mutations in *WT1* may lead to the development of Wilms" tumor in DSD patients; therefore, it is important to identify the presence of mutations by genetic testing in Sri Lanka to plan appropriate follow ups of these children. A larger cohort study is encouraged to determine the prevalence of *WT1* mutations in DSD children.

Keywords: *46,XY DSD, WT1, Wilms' tumor*

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OP 09 (Abstract # 16)

Maternal genetic affinities of Sri Lankan pre-historic and modern populations with the populations in the Eastern world and Australia

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Around 60-70,000 years ago, anatomically modern humans (AMH) migrated out of the African continent to populate rest of the globe. Archaeological evidence indicates the presence of AMH in Sri Lanka and Australia about 45,000 years before present (ybp). The oldest AMH skeletal remains from South Asia dated to about 37,000 ybp (Balangoda man) are reported to share morphological traits with Sri Lankan Adivasi (Vedda) and early inhabitants of Australia. In addition to the Indian subcontinent, Southeast Asia is thought to have contributed to peopling of Sri Lanka. Hence, we attempted to understand the maternal genetic affinity of Sri Lankan prehistoric individuals, Adivasi and Sinhalese with the Aboriginal Australians and Eastern populations using complete mitochondrial (mt) sequences. Sequences of Sri Lankan pre-historic individuals (n=2), Ratugala Adivasi (n=5), and Sinhalese (n=5) were from our ongoing study. Sequences from South Asia (n=16), Andamanese, and Nicobarnese (n=2 each), Southeast Asia (n=21), China (n=8), Papua New Guinea, and Australia (n=7) were from published data. The sequences were first aligned against the revised Cambridge Reference Sequence using MUSCLE. A Neighbor-Joining phylogenetic tree was then constructed from aligned sequences with a 1000 bootstrap (Mega software); the outgroup being an African mtDNA sequence. The phylogenetic tree showed three main clusters. Pre-historic samples clustered mostly among other South Asians including a Sinhalese cluster. Sinhalese showed a closer maternal affinity to South Asians and Southeast Asians. One Adivasi (R haplogroup) showed closer affinity to South Asians, Southeast Asians and Nicobarnese. Another Adivasi (West Eurasian U clade) showed closer affinity to South Asians (Pakistanis and Bangladeshis) and to modern and ancient Aboriginal Australians. A maternal gene flow a) between Sinhalese and, South and Southeast Asians; b) between Ratugala Adivasi and Nicorbanese as well as Australian aborigines or common source populations for respective groups can thus be suggested.

Keywords: Human migration, Sinhalese, Adivasi, South Asia, Southeast Asia, Aboriginal Australian

Acknowledgements: This work was supported by National Research Council (NRC17042) and this work constitutes a part of the PhD studies of author Fernando AS.

OP 10 (Abstract # 35)

Mitogenome diversity in Sinhalese and indigenous Vedda population in Sri Lanka

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Sri Lanka, a tropical island which is located at the Southern tip of the Indian subcontinent, has immensely contributed to human migration since prehistoric times, but inadequately represented in evolutionary studies. Due to its strategic location in the Indian Ocean, the country has witnessed continuous population movements, eventually leading to multiple ethnicities with diverse religions and traditions. Most proto-historic and historic migrations were male-dominated, however, records show that simultaneous and parallel female migrations have also taken place. To understand the maternal migrations, 31 complete mitochondrial genomes of unrelated individuals from Sinhalese (N=16); the major contemporary ethnic group in Sri Lanka, and Adhivasi (Vedda) population from Dambana (N=4) and Hennanigala (a Vedda community who belonged to Dambana- Mahiyangana Adhivasi population and were relocated due to Mahaweli development program in 1983) (N=11) were sequenced using the Sanger sequencing technique. High maternal diversity was observed in studied populations where major haplogroup M is predominant in Sinhalese while U and R haplogroups are predominant in the Vedda population. Five novel sub-haplogroups were identified in U7a2, R6b, U2a1a, R5a2b and M65a+@16311 branches which further differed or rearranged into subclades U7a2b1, R6b1, U2a1a2, R5a2b5* and M65a3. The presence of distinctive haplogroups may indicate early migrations and evolutionary adaptations of the of the two populations in the country. The Fixation Index (Fst) and Analysis of Molecular Variance (AMOVA) results indicate a higher variance within populations. The preliminary observations highlight the necessity of extensive studies in the two groups together with other contemporary populations to understand the peopling of Sri Lanka.

Keywords: Sinhalese, Adivasi Vedda, complete mtDNA, novel haplogroups

Acknowledgements: This work constitutes a part of the PhD studies of author Welikala AHJ.

OP 11 (Abstract # 2)

Selective anti-breast cancer activity of endophytic fungi isolated from *Rhyzophora apiculata*

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Rhyzophora apiculata is a mangrove plant that is reported to have anticancer activity. This study was conducted to determine the anti-breast cancer activity of endophytic fungi isolated from *R. apiculata.* Two fungal strains (Rha/S/A_1 and Rha/S/A_2) were isolated from the stem of the plant, and morphologically differentiated and cultured in large scale using a liquid culture medium. The freeze-dried cultures (4.5 L) were subjected to sequential extraction, in dichloromethane (DCM) and methanol (MeOH). The cytotoxicity of extracts was examined using Sulforhodamine B assay against breast cancer cells MCF-7 (ER-positive), MDA-MB-231 (triple-negative) and normal mammary epithelial cell line MCF-10A at 24, 48 and 72 h post-incubation periods. Pro-apoptotic effect on the cancer cells was determined using Caspase-Glo® 3/7 assay. The antioxidant properties of the anti-breast cancer extract were evaluated using Ferric reducing antioxidant power (FRAP) and 2, 2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity assays. Molecular identification was carried out for the fungal strain that is cytotoxic to breast cancer cells by sequencing the internal transcribed spacer (ITS) region with ITS1F and ITS4S primers. Based on Sulforhodamine B assay Rha/S/A_1 was cytotoxic to the MDA-MB-231 cell line (IC_{50} <100 µg/ mL) and molecular identification showed that it belongs to the *Neofusicoccum sp*. The DCM extract of *Neofusicoccum sp* exerted selective anti-breast cancer activity on the MDA-MB-231 cell line with half-maximal inhibitory concentration (IC_{50}) = 69.32, 50.68 and 32.93 µg/ mL at 24, 48 and 72 h post-incubation respectively. The increased caspase 3/7 activity confirmed the pro-apoptotic effects of the extract. However, extracts have no potent antioxidant properties (DPPH, EC_{50} >100 µg/ mL and FRAP <10 mg Trolox equivalents/g). The results confirmed the anti-breast cancer property of the endophytic fungi *Neofusicoccum sp*. Isolation of the active cytotoxic compounds in this extract may be useful in drug development for triple negative breast cancer.

Keywords: anti-breast cancer activity, *Neofusicoccum sp*, triple negative breast cancer, endophytic fungi, *Rhyzophora apiculata*

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OP 12 (Abstract # 4)

Selective cytotoxicity of marine macroalgae extracts on oral cancer cells (UPCI:SCC 090 and UPCI:SCC 152)

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The prevalence of oral cancer is high in South and Southeast Asia. Conventional cancer therapies have limitations, thus demanding novel drug discovery. Marine macroalgae are a potential source of such novel drugs. We evaluated the cytotoxic properties of three marine macroalgae species, *Sargassum polycystum* (collected from Morawala), *Sargassum* sp. and *Padina antillarum* (collected from Uswetakeiyawa) on oral squamous carcinoma cells (UPCI:SCC 090 and UPCI:SCC 152) and normal human gingival fibroblast cells (HGF-1).The dried macroalgae were extracted sequentially into five different solvents (hexane, chloroform, ethyl acetate, methanol and water) with the aid of sonication. The cytotoxicity of each extract on oral cancer cell lines was determined using a Sulforhodamine B (SRB) assay. Cells were treated with different concentrations of algae crude extracts (25, 50, 100 and 200 µg/mL in triplicates), and an SRB assay was carried out 48 h post-incubation. Algae extracts with half-maximal inhibitory concentration (IC_{50}< 100 µg/mL) were considered as active. According to the results, water extract of *Sargassum* spp. (IC_{50} - 27.59 µg/mL), ethyl acetate and methanol extracts of *Padina antillarum* (IC_{50} - 98.81 and IC_{50} - 52.93 µg/mL respectively) exerted potent cytotoxic effects against UPCI:SCC 090 cancer cells while chloroform and ethyl acetate extracts of *Sargassum polycystum* (IC_{50} - 66.24 µg/mL and IC_{50} - 65.48 µg/mL respectively) demonstrated potent cytotoxic effects against UPCI:SCC 152 cancer cells. These extracts were less toxic (IC_{50} > 100 µg/mL) to non-cancerous cells (HGF-1). Considering the promising selective cytotoxic properties shown by the active extracts on oral cancer cells while being less toxic to non-cancerous cells, isolating active compounds from marine macroalgae may lead to the development of novel beneficial chemotherapeutic agents.

Keywords: marine macroalgae, cytotoxicity, UPCI:SCC 090, UPCI:SCC 152 , HGF-1

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OP 13 (Abstract # 8)

Acetylcholinesterase inhibitory activities of *Jasminum multiflorum, Jasminum rottlerianum, Darcena sanderiana and Sansevieria zeylanica*

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Acetylcholinesterase (AChE) inhibitors have been used for the treatment of Alzheimer's disease and other memory-related disorders for years in various parts of the world. Medicinal plants are known to biosynthesize a wide variety of biologically active secondary metabolites and is therefore considered as a potential source for the discovery of new anti-acetylcholinesterase active compounds. *Jasminum multiflorum, Jasminum rottlerianum, Darcena sanderiana, Sansevieria zeylanica* have been used in traditional medicine to treat various diseases including cognitive disorders. This study was carried out to evaluate AChE inhibitory properties of the organic extracts of the above-mentioned plants. Air dried, powdered samples from different plant parts (leaves, stem bark, roots, and flowers) were sequentially extracted with 3 solvent systems (CH_2Cl_2, Methanol: CH_2Cl_2-1:1 and Methanol) and combined to yield a total extract of the individual plant part. The organic extracts were evaporated to dryness and redissolved in a methanol-water mixture (7:3), and these mixtures were tested for AChE inhibiting activity using Ellman's method in 96-well microplates. Donepezil (AChE IC_{50} value = 34 nM) was used as the standard acetylcholinesterase inhibitor and all the tests were done in triplicates. Out of the 12 organic extracts tested, potent AChE inhibitory activities were shown by the flower and leaf extracts of *J. multiflorum* with IC_{50} values of 135±0.4 µg/mL and 180±0 µg/mL, respectively. Furthermore, *J. rottlerianum* flower extract and leaf extract exhibited significant AChE inhibiting activities with IC_{50} values of 180±1.4 µg/mL and 190±0.8 µg/mL, respectively. Hence, it can be concluded that *J. multiflorum* and *J. rottlerianum* leaves and flowers possess anti-cholinesterase activity, which can be investigated to isolate possible drug leads with anti-acetylcholinesterase activity.

Keywords: Acetylcholinesterase*, Darcena sanderiana, Jasminum multiflorum, Jasminum rottlerianum, Sansevieria zeylanica*

OP 14 (Abstract # 12)

Determination of anti-tubercular activity of selected phytochemicals using molecular docking

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Multi-drug resistant strains of *Mycobacterium tuberculosis* are currently a major challenge in the treatment of tuberculosis, leading to rising tuberculosis-related mortality around the world. Globally, 1.4 million deaths occurred in 2019, a number that rose to 1.5 million deaths in 2020. Discovery and development of new anti-tubercular drugs have become essential due to this pattern of existing treatments losing efficacy due to drug resistance. In this study, phytochemicals were blind-docked using AutoDock 4.2.6, which was selected based on its compatibility with windows 10, 64-bit processor and internet speed of 21 Mbps. Methoxy mycolic acid synthase 4 (PDB ID:2FK8) is a fatty molecule inside the mycobacterium cell wall which makes bacteria to subvert and hide from the immune system. The 2FK8 file was downloaded from RCSB PDB. Receptor preparation was carried out by removing water, adding hydrogen molecules, removing heteroatoms, and adding Kollman charges. Ligand preparation was performed by retrieving 3D structures from PubChem in SDF format and converting it to PDB format in OpenBabel. Grid box was generated using grid box parameters (122×124×118). Autodock and autogrid were executed separately by setting Lamarckian genetic algorithm at 50 runs, for a population size of 300. The free binding energies were found as follows: ecdysone, silymarin, berberine, piperine, curcumin, quercetin, resveratrol and gingerol (-9.12, -9.11, -8.64, -7.96, -7.63, -7.37, -7.16, -6.18 kcal/mol) respectively. The best binding energy was determined using lowest value (ecdysone = -9.12 kcal/mol). Inhibition constant (ki) values of berberine, ecdysone, and silymarin were considered as non-potent inhibitors (ki> 100µM). Best docking pose and interactions were acquired by BIOVIA Discovery studio and Ligplot$^+$. Silymarin (*Andrographis paniculata)*, piperine (*Piper longum)*, berberine (*Berberis aristata)* and curcumin (*Curcuma longa)* can be extracted from available plants in Sri Lanka using aqueous an alcoholic fermentation technique. Further experimentation needs to be carried out to prove efficiency.

Keywords: multi- drug resistant, methoxy mycolic acid synthase 4, Lamarckian genetic algorithm, blind dock

OP 15 (Abstract # 17)

Protein-ligand docking for the identification of ligand binding sites and novel therapeutics for breast cancer

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Breast cancer, the most common cancer in women, is caused due to the uncontrolled growth of breast cells, giving rise to tumours. Current therapy includes hormonal therapy, in which receptors are targeted for their downregulation or inhibition by the action of drugs. The wide use of these drugs have worked well against tumours, however, adverse effects like tumour relapse and resistance in patients, remain the primary cause of death in women. This urges us to explore alternative therapy, with fewer side effects and higher drug efficiency to effectively treat breast cancer. Naturally occurring phytochemicals have recently shown great potency as therapeutic agents. To study this, docking studies were carried out to analyse the interaction of phytochemical ligands against the estrogen receptor, with the aim of identifying potential anticancer drugs. The drug-likeness property of the phytochemicals was evaluated for any adverse effects by applying Lipinski's rule of five using SwissADME, and the six phytochemicals - Pristimerin, Azatoxin, Sophoridine, Alpha-Peltatin, Camptothecin, and Emetine- were chosen. The 3D structure of estrogen receptor (ER) was retrieved from RCSB PDB (ID:2IOK) and the phytochemical ligands were downloaded from NCBI PubChem. The receptor and ligand were docked using blind docking in AutoDock 4.2.6. The docking area was centered at x, y and z coordinates of 14.468, 25.978 and 41.174 respectively and the docking was carried out with 50 GA runs for a population size of 300. The lowest binding energies and inhibition constant of the docked poses, signifying a stable complex, were analysed. Based on the results, Camptothecin, Azatoxin and Pristimerin came up with the lowest binding energies of -9.00, -8.88, -8.71 kcal/mol respectively. These results confirm that these agents could be promising anti-cancer agents in the treatment of breast cancer.

Keywords: blind docking, estrogen receptor, Camptothecin, drug-likeness

OP 16 (Abstract # 23)

Isolation of an anti-cancer compound from *Mangifera zeylanica* leaves and investigation of potential cytotoxic effects

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Lung cancer is a frequently identified cancer worldwide. Of the two types of lung cancer, Non-Small Cell Lung Cancer (NSCLC) is most commonly identified. Although surgical treatments show acceptable results, chemo- and radio-therapies are required in metastatic cases. Notably, chemo- and radio- therapies cause severe side effects, necessitating the need of new treatment strategies. The use of plant extracts or plant derived compounds holds great potential in the field of anti-cancer drug discovery. *Mangifera zeylanica* (Etamba, family: Anacardiaceae) is a plant found commonly in Sri Lanka. This study aims to isolate potential anti-cancer compound/s from *M. zeylanica* leaves and to evaluate their cytotoxic and apoptotic effects in non-small lung cancer cells for the first time. A compound (A1X) was isolated from the chloroform extract of *M. zeylanica* leaves using silica-gel column chromatography followed by preparative reversed phase high performance liquid chromatography (HPLC). Cytotoxic effects of A1X were investigated using the Sulforhodamine B (SRB) assay. The effects of A1X on colony formation and cell migration were investigated by colony formation and wound healing assays, respectively. Ethidium Bromide/Acridine Orange (AO/EB) staining was employed to assess the potential apoptotic effects of A1X. The compound A1X showed cytotoxicity in NCI-H292 cells with an IC_{50} of 5.46 µg/mL following 24 h exposure. In addition, A1X inhibited colony formation and migration of NCI-H292 cells. AO/EB staining showed that A1X can induce apoptosis in NCI-H292 cells. Structure elucidation of A1X and mechanistic anti-cancer studies are in progress.

Keywords: lung cancer, NSCLC, *Mangifera zeylanica,* NCI-H292

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OP 17 (Abstract # 26)

Protein-ligand docking of phytochemicals against Alzheimer's disease

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The development of Alzheimer's disease (AD) has been associated with the formation of beta-amyloid protein (β-amyloid) aggregates in the brain. Similarly, the presence of ApoE4 gene have also been identified to increase the risk of AD. However, clinical symptoms of AD are detected long after neuronal damage has occurred. At present there is no cure for AD and treatment methods focus only on reducing the symptoms. Aducanumab is the only current FDA-approved drug to target amyloid plaques. Most research aimed at inhibiting amyloid formation have been unsuccessful due to an inability to pass through the blood-brain-barrier. Plant-based compounds facilitate permeation through the blood-brain-barrier and can potentially inhibit AD-causing proteins with minimal side effects. Identifying the best binding sites for ligands using protein-ligand docking can provide an opportunity to discover novel drugs that prevent or cure AD in its earlier stages. In this study, existing drugs for acetylcholinesterase (AChE), clinical trial drugs and five phytochemicals from various plant sources were retrieved from NCBI PubChem. The receptors β-amyloid and ApoE4 were retrieved from RCSB PDB. Docking was performed using AutoDock via 1.1.2. ADMET properties of the ligands and were examined using SwissADME. Among the docked phytochemicals, the best binding pose for β-amyloid and ApoE4 were observed in Hesperidin, with a binding affinity of -7.5 kcal/mol. Docking of β-amyloid with Asiatic acid from *Centella asiatica*, Kuromanin and Urolithin A, from *Punica granatum*, showed binding affinity of -6.4, -6.9, -6.2 kcal/mol respectively. Similarly, ApoE4 docking with Asiatic acid, Kuromanin and Urolithin A showed binding affinity of -7.0, - 7.3, -6.8 kcal/mol respectively. The lowest affinity of -4.4 kcal/mol for β-amyloid and -4.8 kcal/mol for ApoE4 was observed in Citral, from *Cymbopogon citratus*. In conclusion, these phytochemicals demonstrate potential inhibiting properties against AD receptors. Further clinical studies and in vitro experiments are required to determine their efficacy against AD.

Keywords: Alzheimer's disease, β-amyloid protein, ApoE4, phytochemical, neuroprotection

OP 18 (Abstract # 28)

Preliminary study on phytochemical analysis and GC-MS fingerprints of Sri Lankan traditional polyherbal drug "Panu"

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"Hela Vedakama" is a traditional form of an indigenous medical system that uses specific Polyherbal formulations for various ailments including viral and bacterial infections with considerable success. One such Polyherbal formulation for the treatment of viral and bacterial infections is "Panu". The detailed view of phytochemicals and their bioactivity of this drug is poorly understood. Therefore, this study aimed to investigate the phytochemical profile and the scope of their bioactivity. Aqueous extracts were concentrated based on the lyophilization technique. Total Phenolic Content (TPC) was determined using Folin-Ciocalteu assay and results expressed as Gallic Acid Equivalents (GAE). The DPPH radical scavenging assay was performed to determine antioxidant activity using ascorbic acid as the reference standard. The IC_{50} value of extracts was calculated from the percentage scavenging activity. GC-MS fingerprinting study was also carried out to detect phytochemicals in an ethanol extract of the polyherbal drug. All the experiments were performed in triplicates and a linear regression model was used to analyze the data. The total phenol content of aqueous extracts of "Panu" was found to be 7.88 ± 0.19 GAE, while the extract shows IC_{50} = 367.00 ppm for DPPH radical scavenging activity (compared with Ascorbic acid, IC_{50}= 37.42 ppm). Furthermore, the GC-MS fingerprinting technique revealed the presence of Phenol derivatives of Phenol,2,6-bis (1,1-dimethyl ethyl)-,1,4- benzene dicarboxylic acid and Benzene propanoic acids. In conclusion, these results show that "Panu" possesses considerable antioxidant activity, which necessitates further cytotoxicity studies.

Keywords: GC-MS fingerprinting, bioactive compounds, antioxidant activity, IC_{50}

OP 19 (Abstract # 30)

Virtual Screening and Molecular Dynamics Based Identification of Bismahanine as a Potential Anti-Aging Compound

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Since the middle of the 19th century, human life expectancy has been steadily increasing in many parts of the world, including Sri Lanka. At the age of 60 years or older, individuals become more prone to chronic illnesses with a rising burden of multimorbidity. Hence, the identification of new anti-aging compounds that might be present in common herbs and food plants will open up avenues for formulating effective and readily available anti-aging formulations. To identify new anti-ageing phytochemicals, a library of 1426 plant secondary metabolites was constructed *in silico,* based on the previous research work of the Institute of Biochemistry, Molecular Biology and Biotechnology (IBMBB) and by carrying out database and literature searches. Phytochemical library thus constructed was screened against validated anti-aging drug targets mTOR1, sirtuin-1, FOXO3, elastase, collagenase, hyaluronidase-1 and myeloperoxidase. Absorption, distribution, metabolism, excretion, and toxicity (ADMETox) parameters were predicted in silico to determine the drug likeliness of identified potential anti-aging compounds. To verify the findings, molecular dynamic simulations were carried out for potential hits. Possible other targets of identified potential anti-aging compounds were predicted by target fishing and a network pharmacology approach. Based on the binding affinity values, 35 hits were selected for interaction analysis and ADMETox prediction. Of the 35 compounds, compound 23 (bismahanine) of *Murraya koenigii* was predicted to have very high anti-aging potential by eliciting required inhibitory and activator responses. Molecular dynamics simulations confirmed that the complexes formed by bismahanine with mTOR1, Sirtuin-1, and FOXO3, were stable up to 100 ns in aqueous environment. Target fishing and network pharmacology analysis provided limited evidence for potential off-target effects of bismahanine. Overall results indicate that bismahanine may be a natural compound with potent anti-aging properties. However, results should be experimentally validated through in vitro and in vivo experiments.

Key words: Virtual Screening, Drug Discovery, Medicinal Plants, Anti-Aging, Bismahanine

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OP 20 (Abstract # 31)

In silico Identification and *In Vitro* Validation of Alpha Hederin as a Wnt/β catenin pathway inhibitor in breast cancer stem cells

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Breast cancer stem cells (bCSCs) play a vital role in tumor cell proliferation, metastasis, recurrence and chemoresistance in breast cancer. Abnormal activation of Wnt (wingless)/β-catenin pathway signaling increases bCSC stemness. β-catenin proteins of the signaling pathway binds to T-cell factor-4 (Tcf4) DNA binding proteins playing a critical role in the downstream activation of proliferative genes in response to upstream Wnt/β-catenin signaling. Thus, the purpose of the present study was to identify a small molecule inhibitor that can effectively disrupt β-catenin/Tcf4 interaction. Molecular docking studies were performed using 1000 natural or synthetic small molecules as ligands and β-catenin (PDB entry 1JPW) as the target. The best hit compound alpha-hederin (AH) with binding energy of -8.2 kcal.mol^{-1} was further subjected to interaction studies and in silico drug likeness analysis. Interestingly, AH follows the drug likeness properties and it was predicted to be non-carcinogenic, and non-toxic. Furthermore, anti-proliferative activity and apoptotic effects of AH was studied *in vitro* on bCSCs using WST-1 and caspase 3/7 assays, respectively. AH significantly decreased the viability of bCSCs in a dose and time dependant manner. In addition, AH suppressed the mRNA expression of Wnt/β-catenin downstream target genes *Cyclin D1* and *CD44* and up-regulated the mRNA expression of the tumor suppressor gene *p53*. Collectively, results of this study demonstrate that AH could serve as a potential inhibitor of bCSCs growth by down regulating the Wnt / β-catenin signaling pathway.

Key words: In silico, In vitro, Breast Cancer Stem Cells, Alpha Hederin, Wnt/β-catenin

Acknowledgements: This work was supported by Institute of Biochemistry, Molecular Biology and Biotechnology (IBMBB), University of Colombo.

OP 21 (Abstract # 33)

Antibacterial properties in "*Madhuca longifolia*" leaves and seeds extractions against selected Gram negative and positive microbial strains.

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Infections caused by bacteria showing antibacterial resistance is a major cause of death in the developing world. As a solution for antibiotic resistance, researchers are searching for alternatives to antimicrobials including natural phytochemicals found in plants. Previous research has shown the antibiotic properties of *Madhuca longifolia*, which belongs to the family *Sapotaceae*. Ethanolic and methanolic extractions of the plant were tested for inhibitory activity against *Staphylococcus aureus* and *Escherichia coli* using the antibiotic sensitivity test (ABST), which was carried out by well diffusion technique in Mueller Hinton agar media, and then the diameters of zone of inhibition were measured and analysed according to The Clinical Laboratory Standards Institute (CLSI) standards. Two concentrations (50mg/ml, 100 mg/ml) of plant extract were used. Both the ethanolic and methanolic extracts of *M. longifolia* seeds and leaves showed a higher zone of inhibition against *S.aureus*. The maximum diameter zone of inhibition was shown by the *M. longifolia* ethanol extract from seeds against *S. aureus* (18.00±0.81 mm), and the minimum zone of inhibition was shown by the *M. longifolia* ethanol extract from seeds, 50mg/ml against *Escherichia coli* (11.33±0.47 mm). Gentamycin in mg/ml concentration was used as the positive control, while DMSO served as the negative control. The results were analyzed using two-way ANOVA in Prism software and the difference was not significant. Since zones of inhibition were observed, it can be concluded that the plant contains antimicrobial compounds that are responsible for the observed antibacterial activity. Therefore, it is possible to state that this study has achieved the objectives that were proposed. It is recommended that the study should be repeated using quantitative analysis, different solvents and different microbial strains.

Keywords: *Madhuca longifolia*, antibiotic resistance, antimicrobial properties, Antibiotic Sensitivity Test (ABST)

OP 22 (Abstract # 37)

Effect of a polyherbal formulation in Sri Lankan market on the mRNA expression and secretory levels of inflammatory cytokines in THP-1 derived human macrophages

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Cytokines play an important role in mediating inflammation, hence forming the first line defense towards infectious pathogens. Link Samahan® (LS) is a well-known polyherbal formulation used in Sri Lanka as well as internationally for prophylaxis against cold and cold related symptoms. This study was designed to evaluate the effect of LS on both, expression and secretion of pro-inflammatory cytokines [interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), interferon-gamma (IFN-γ)] and anti-inflammatory cytokines (IL-10) in THP-1 derived human macrophages (THP-1-M). THP-1 cells were differentiated into macrophages using phorbol 12-myristate-13-acetate. THP-1-M was treated with increasing concentrations of LS and the stimulation was followed with the addition of 1 µg/ml lipopolysaccharide (LPS). The effect of LS on cytokines in LPS-stimulated THP-1-M were assessed by measuring the cytokine levels in culture supernatant and by quantifying mRNA expression by encoding for cytokine genes for IL-6, TNF-α, IFN-γ and IL-10. LS concentration from 30.52 to 976.56 µg/ml were determined as suitable, being non-toxic to THP-1-M using both cell viability and functionality assays. In LPS-stimulated THP-1-M, LS has significantly increased both, mRNA expression and secretory levels of IL-10 in a dose-dependent manner ($r=0.975$; $p=0.001$). LS treatment of THP-1-M had also significantly suppressed the secretion and downregulated the expression of mRNA of IL-6 ($r=-0.909$; $p=0.012$) and TNF-α ($r=-0.846$; $p=0.034$) in a dose-dependent manner. Additionally, LS showed a tendency to decrease the expression and secretory levels of IFN-γ ($r=-0.743$; $p=0.091$). These results suggest that LS has induced mRNA expression as well as secretion of anti-inflammatory cytokine (IL-10) while suppressing both expression and secretion of pro-inflammatory cytokines (IL-6 and TNF-α) in human macrophages, which together contributes to its anti-inflammatory properties. Further, the upregulation of IL-10 (anti-pyretic) and simultaneous downregulation of IL-6 and TNF-α (pyrogens) further validate the previous claim on the use of LS as a prophylactic formulation against cold related symptoms.

Keywords: Cytokines, Link Samahan®, IL-6, IL-10, TNF-α

Acknowledgements: This work was supported by the IBMBB & Link Natural Products (Pvt) Ltd and constitutes a part of the PhD studies of author Ranaweera BVLR.

OP 23 (Abstract # 38)

Immunostimulatory effect of a polyherbal formulation in the Sri Lankan market: enhancement of IgG expression levels

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Link Samahan® (LS) is a polyherbal formulation used in Sri Lanka and internationally as a prophylaxis against cold and cold related symptoms. The objective of this study was to observe the effect of LS in stimulating the humoral immune response; specifically on inducing antibody responses: IgM during primary immune responses and IgG and IgA during secondary immune responses. Twelve Wistar rats were placed into two groups (n=6). Both groups were immunized with BSA as a protein antigen on day 1 and day 15. The test group was orally administered with LS, and the control group was treated with water for five consecutive days after the 1st dose and the booster dose of BSA. Rat peritoneal cells (RPC) were collected from both groups on 0-8 and 14-22 days with a one-day gap in-between. Quantitative RT-PCR was performed using RNA extracted from RPC and gene specific primers to determine the expression of mRNA encoding IgM, IgG and IgA. The expression of IgM in the LS-treated group reached a significantly higher level during the primary antibody response on day 6-8 (2.73-2.79 folds; $p<0.0001$) compared to control. The IgG response of LS-treated animals exhibited a marked increase during the secondary antibody response (4.17 folds; ($p<0.0001$) by day 20-22. The IgA response in the LS-treated group was shown by a higher trend in its expression (1.75 folds; $p=0.114$) between day 6-8. The expression of all three types of immunoglobulins (IgA, IgG and IgM) were higher in the LS-treated group. There was a significant and marked increase in IgG levels in the LS-treated group reflecting its immunostimulatory and boosting effect compared to the control group. Therefore, these findings show that LS could be considered as a booster of humoral immunity.

Keywords: immunostimulation, Link Samahan®, IgA, IgG, IgM

Acknowledgements: This work was supported by the IBMBB & Link Natural Products (Pvt) Ltd and constitutes a part of the PhD studies of author Ranaweera BVLR.

OP 24 (Abstract # 48)

Cytotoxicity of *Allophylus cobbe* extracts against human hepatocellular carcinoma (HepG2) cells

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Despite limited scientific evidence, use of medicinal plants in cancer treatment has a long and recorded history. This study was carried out to investigate the possible *in vitro* anti-liver cancer effects of *Allophylus cobbe*, a native medicinal plant primarily used by Sri Lankan traditional medical practitioners to treat stomach ache. Dried leaves and bark of *A. cobbe* (5g) were sequentially extracted to hexane, dichloromethane, ethyl acetate and methanol. Hepatocellular carcinoma (HepG2) cells cultured *in vitro* were treated with *Allophylus cobbe* extracts for 48 h, and cytotoxicity was evaluated using the sulfohordamine B (SRB) assay. Active extracts were used to evaluate toxicity against *in vitro* cultured non-cancerous liver cells (THLE-3). Ferric reducing antioxidant power (FRAP), 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2-azino-bis (3-ethylbenzothiozoline-6-sulfonic acid (ABTS) assays were carried out to determine the antioxidant activity of the extracts. Total flavonoid and total polyphenolic contents of the extracts was determined. All four of the leaf extracts tested exerted potent cytotoxicity (IC_{50} values 6.8, 9.4, 11.3 and 20.0 µg/mL respectively) while none of the bark extracts showed cytotoxicity against HepG2 cells (IC_{50}>100 µg/mL). All active extracts were also highly selective towards HepG2 cells (IC_{50}> 100 µg/mL for THLE-3). Further, methanol extracts of leaves and bark exhibited moderate radical scavenging activity in the DPPH assay (EC50: 72.78±21.12 and 49.58±6.68 µg/mL), FRAP assay (174.15±22.87 and 313.63±35.31 mg/g trolox equivalents) and ABTS (EC_{50}: 20.87±2.81 and 29.75±1.42 µg/mL). The methanol extract of leaves and bark also exhibited a comparatively high phenolic content with 89.26±6.90 and 82.43±8.60 mg/g gallic acid equivalents while dichloromethane and ethyl acetate extracts of leaves contained a considerable amount of total flavonoids (123.42±3.93 and 84.24±6.35 mg/g quercetin equivalents respectively). Overall, these results suggest that *A. cobbe* is a good source to develop treatments for hepatocellular carcinoma.

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OP 25 (Abstract # 50)

Effect of *Vernonia zeylanica* on non-IgE mediated degranulation and histamine release by RBL-2H3 cells in vitro

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Allergic reactions are on a rise in Sri Lanka and the world over, and its treatment relies on expanded use of anti-allergic drugs ranging from simple anti-histamines to mast cell stabilizing agents which inhibit the release of mediators including histamine. Mast cell degranulation occurs via both IgE-mediated and non-IgE mediated pathways. This study aimed to screen the (non-IgE mediated) anti-allergic effects of extracts of *Vernonia zeylanica* using histamine release from RBL cells. *In vitro* cultured RBL-2H3 cells were treated with 500 ng/ml of compound 48/80 to induce non-IgE mediated degranulation and release of histamine via Ca^{2+} influx. The level of histamine released was detected using O-phthaldialdehyde (O-PT) which forms a fluorescent conjugate enabling quantification of histamine using a fluorometric assay. Cromolyn sodium salt, which is a mast cell stabilizer was used as the positive control. The non-toxic concentrations of solvent fractions of methanol (Vz-met), hexane (Vz-hex), ethyl acetate (Vz-EtOAC) and crude extract (VZ-crude) of *V. zeylanica* were screened for their inhibitory effects on RBL cell degranulation and histamine release. RBL cells were plated at a concentration of 4 x 10^4 cells/well, treated with either plant extract/positive control for 1 h and interacted with Compound 48/80 for 30 min at 37 °C. Then the percentage degranulation of RBL cells was confirmed by Toluidine blue assay. The positive control, Cromolyn salt showed 87% of mean percentage inhibition on histamine release at 100 µg/ml whereas the *V. zeylanica* extracts showed mean maximum inhibition of 48% at 62 µg/ml of *Vz*-hex, 48% at 31 µg/ml of *Vz*-met, 49% at 15 µg/ml of *Vz*-EtOAC and 51% at 62 µg/ml of *Vz*-crude. These findings emphasize further investigations on compounds responsible for the observed non-IgE mediated histamine release/ degranulation on RBL-2H3 cells and the anti-allergic activity of *V. zeylanica*.

Keywords: non-IgE mediated allergy, basophil degranulation, RBL-2H3 cells, *Vernonia zeylanica*, O-phthaldialdehyde

Acknowledgements: This work was supported by the IBMBB and constitutes a part of the MSc studies of author Kulathunge SSB.

OP 26 (Abstract # 53)

In-vitro Anti-inflammatory Properties of the Ethyl Acetate Soluble Proanthocyanidins (EASPA) from the Immature Inflorescence of *Cocos nucifera* L.

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The immature inflorescence of *Cocos nucifera* L. (IF) is widely used in traditional medicinal practices including ayurveda in Sri Lanka for the treatment of menorrhagia, a common gynecological disorder in women. The orange color variety aurantiaca which is commonly known as "*thembili*" in sinhala is used for this purpose. The IF consists of proanthocyanidins predominantly. Progestogenic activity of EASPA have been previously reported. This finding is very significant because in western medicine synthetic progesterones are used to treat menorrhagia and EASPA are chemically different to synthetic progesterons. A strong connection between inflammation and menorrhagia has been reported in literature and therefore, anti-inflammatory properties of EASPA was investigated in the present study using published *in- vitro* anti- inflammatory assay protocols. Assay for the inhibition of heat and hypotonic induced heamolysis of erythrocyte membranes were performed using different concentrations of EASPA varying from 0.2– 0.9 mg/mL whereas concentrations varying from 0.3 – 2.0 mg/mL were used in proteinase inhibitory assay protocol. Diclofenac sodium was used as the standard drug in all assay protocols. The half maximal inhibitory concentration (IC_{50}) for both EASPA and the standard drug was calculated in non-linear regression analysis. EASPA showed a significant (p<0.05) inhibitory effect on proteinase activity by giving the IC_{50} value of 1.1±0.0 mg/mL. The IC_{50} value for the standard drug was 1.4±0.0 mg/mL. EASPA exhibited inhibitory effects on both heat and hypotonic induced heamolysis of erythrocyte membranes with IC_{50} values of 0.5 ±0.0 mg/mL. The IC_{50} values of the standard drug were obtained as 0.4±0.0 mg/mL for inhibition of heat induced heamolysis and 0.5±0.0 mg/mL for hypotonic induced heamolysis of erythrocyte membranes. These findings strongly suggest that EASPA can mediate anti-inflammatory properties and further studies would be needed to develop a potential herbal remedy to treat women who are suffering from menorrhagia world over.

Keywords: *Cocos nucifera* L. proanthocyanidins, menorrhagia, anti-inflammatory assay

Acknowledgements: This work was supported by University Research Grant (ASP/01/RE/SCI/2018/20)

OP 27 (Abstract # 54)

Effectiveness of *Aegle marmelos* (Bael) fruit and leaf extracts against selected *Candida* species

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The incidence of opportunistic fungal pathogens has increased, resulting in high mortality rates in hospitalized, immune-compromised patients. *Candida* species are among the most common causes of nosocomial fungal infections. Due to the overuse of antifungal medications, these organisms have developed resistance to conventional antifungal drugs, necessitating the development of novel anti-candidal therapeutics with different chemical compositions and modes of action from alternative sources such as plants. Therefore, plants with known antifungal activity in folk medicinal practice need to be evaluated for their anti-candidal potential. The current study was undertaken to investigate the anti-candidal activity of *Aegle marmelos* fruit and leaf extracts against three standard *Candida* strains, viz. *Candida albicans* (ATCC 10232), *Candida krusei* (ATCC 200917) and *Candida parapsilosis* (ATCC 22019). The agar well diffusion method was used to evaluate the anti-candidal activity of methanolic extracts with 80% dimethyl sulfoxide (DMSO) as the negative control and standard fluconazole as the positive control. The growth of all three *Candida* strains was inhibited by both leaf and fruit extracts of *A. marmelos*. The mean inhibition zone diameters of *C. albicans, C. krusei* and *C. parapsilosis* for *A. marmelos* leaf extract were 19.67±0.58 mm, 20.00±0.00 mm and 16.67±0.00 mm respectively while mean inhibition zone diameters of 18.00±0.00 mm, 19.67±0.58 mm and 13.67±0.58 mm were obtained against the same organisms for the fruit extract. Mean inhibition zone diameters of 40.33±0.58 mm, 42.00±0.00 mm and 37.67±0.58 mm were obtained for the fluconazole control. No inhibition was observed in all three species for the negative control. The results of preliminary screening reveal that both the leaf extract and the fruit extract of *A. marmelos* have the potential to be developed as anti-candidal therapeutic agents.

Keywords: anti-candidal, antifungal resistance, *Candida*, natural products

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OP 28 (Abstract # 7)

Identification of potential therapeutic agents for COVID-19 through site-specific protein-ligand docking

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The enduring COVID-19 pandemic caused by SARS-CoV-2 has wreaked havoc across the entire globe, claiming millions of lives and disrupting livelihoods since December 2019. Despite the availability of vaccines and repurposed drugs for COVID-19, this deadly virus still continues to claim millions of lives. The key issue is the lack of effective and specific drugs for COVID-19. Therefore, this research intends to screen out the potential drugs that effectively inhibit "SARS-CoV-2 M^{pro}", a key enzyme for viral replication, by performing protein-ligand docking using AutoDock 4.2.6 program**.** FDA-approved drugs (nirmatrelvir, clofazimine, darunavir, ribavirin, and remdesivir (control)) and antiviral phytochemicals (meliacinanhydride, maslinic acid, hinokinin, rutin, and arctigenin) were selected as ligands. Docking was performed on a Windows 10-based, 64-bit processor with 23.41 mbps internet. Firstly, the 3D structures of SARS-CoV-2 M^{pro} (PDB ID: 6LU7) and ligands were retrieved from RCSB PDB and PubChem databases, respectively. All ligand data files were converted from SDF to PDBQT format. AutoDockTools was imported to process the protein and ligand structures. Grid parameters were set as follows: Grid spacing = 0.375 Å; Center grid box values for x = -13.156, y = 13.688 and z = 69.379; and Grid size = 60 x 60 x 60. Subsequently, AutoGrid and AutoDock were executed. Hydrogen and hydrophobic interactions were visualized using Discovery Studio Visualizer. Ligands with lowest binding energy and lowest inhibition constant are potential SARS-CoV-2 M^{pro} inhibitors. Based on these criteria, clofazimine was ranked first, followed by maslinic acid and nirmatrelvir, with binding energies of -10.63 (Ki = 0.01619 µM), -9.58 (Ki = 0.09465 µM), and -8.69 kcal/mol (Ki = 0.42435 µM), respectively. In conclusion, these top 3 ligands could be used to treat COVID-19. Additional wet-lab experiments and clinical trials under *in vitro* and *in vivo* conditions are required to corroborate these findings.

Keywords: AutoDock, binding energy, inhibition constant, SARS-CoV-2 M^{pro}

OP 29 (Abstract # 18)

Protein-ligand docking study to identify ligand binding sites against Hepatitis B protein receptor

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Hepatitis B affects about 2 billion people worldwide. The current therapeutic strategies aid in managing the disease but offer no cure. This project was designed to screen for novel lead compounds to discover a drug that effectively targets the hepatitis B core protein (HBc). HBc (PDB ID: 5WRE) was chosen as it is essential for the formation of the viral capsid. Further studies indicate that HBc interacts with covalently closed DNA to promote transcription. Hence inhibition of HBc function can inhibit viral replication. Two FDA drugs, artemisinin and ciclopirox were used as standards. The compounds for screening were, phytochemicals, namely, yuehchukene, myrtillin, curcumin, sanggenol O, chlorogenic acid, helioxanthin, 20-deoxyingenol, nirtetralin, oxymatrine and neolancerin. Autodock 4.2.6 was utilized to conduct blind docking using a Windows 10, 64-bit processor computer. To carry out docking, a grid box was created (x, y, z dimensions= 126, grid spacing= 0.62), followed by the setting of GA runs and population size to 50 and 300 respectively. The protein-ligand complexes were then visualized using BIOVIA. The binding energy values from RMSD tables were used to determine the best docked pose. Based on the binding energy the best docked ligands were yuehchukene, sanggenol O and helioxanthin (-10.56, -10.14, -9.37) kcal/mol, respectively, which were lower than the FDA drugs (artemisinin= -8.71 kcal/mol, ciclopirox= -7.01 kcal/mol). Out of the three best docked ligands yuehchukene had the lowest inhibitory constant followed by sanggenol O and helioxanthin (18.21, 36.8, 134.96) uM respectively. In conclusion yuehchukene and sanggenol O are the most suitable lead compounds as they have a stable binding energy and potent inhibitory constants, while helioxanthin though it has a good binding energy is a poor inhibitor. Additionally, *in vitro* studies must be done by isolating these compounds using ethanolic extraction to better understand their effectiveness and potential toxicities.

Keywords: Hepatitis B core protein (HBc), blind dock, Yuehchukene, Sanggenol O, inhibitory constant

RESEARCH PAPERS-POSTERS PRESENTATIONS

PP 01 (Abstract # 59)

In-house Development of a Rapid Antigen Test for Detection of SARS-CoV-2 Infections

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With the SARS-CoV-2 pandemic, early and rapid diagnosis is essential to prevent disease transmission. While several types of tests are available for SARS-CoV-2 diagnosis, including rapid antigen detection and PCR, commercially available tests are expensive, and the sensitivity of some test kits is limited. The development of an in-house assay which is cost effective and has higher sensitivity would thus be important. We aimed to develop an in-house, rapid test for SARS-CoV-2 antigen detection as a proof of principle for a lateral flow assay, before the rapid antigen test kits were commercially and widely available in Sri Lanka. A total of 30 confirmed samples having PCR cycle threshold (CT) value <25 [n=14; stored in buffer (n=6) and virus transfer media (VTM) (n=8)], 25-30 (n=8 stored in VTM) and >30 (n=8 stored in VTM) were used. Results were compared with a commercially available rapid antigen test kit (Abbott-Panbio). Of the samples with <25 CT, the in-house developed test strips detected 64% (9/14; 64% sensitivity) whereas only 35% (5/14) was detected by the commercial kit (35% sensitivity). Of these 14 samples, those stored in buffer, 50% and 17% were detected by the in-house developed test strips and the commercial kit respectively. Of the samples stored in VTM, a higher positivity rate was detected with the in-house developed test strips (75%) compared to the commercial kit (50%). Similarly, when the samples with CT value 25-30 were tested, 25% were positive with the in-house developed test strips while none were positive with the commercial kit. Both assays did not detect any positives among the samples having CT>30. These preliminary findings are promising as a proof of principle for the further development of a lateral flow based rapid diagnostic device for the detection of SARS-CoV-2 antigen with high sensitivity and specificity.

Key words: SARS-CoV-2, rapid diagnostic test, sensitivity, specificity

Acknowledgements: This work was supported by National Research Council, Rapid Response Grants (Grant no. CVD 20-024).

PP 02 (Abstract 63)

Elevated mRNA expression levels of Cytokine in patients with psoriasis

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Psoriasis is a long-term disease known for its occasional flare ups on the skin, causing great discomfort to the sufferer. This autoimmune disease affects approximately 2-3% of the world's population, independent of age, gender or nationality. The immunopathogenesis of psoriasis revolves around innate immune cells, adaptive immune cells and cytokines. Being a multifactorial disease, psoriasis is triggered by many external factors and stimuli, which activate the immune cells and induce them to secrete inflammatory cytokines, including IL-6, IL-8, IL-10 and TNF-α. Cytokines activate the immune response by recruiting immune cells to the skin and blood, and upregulating the inflammatory cascade, which is a major component of the pathophysiology of psoriasis. After obtaining informed written consent, the patients (n=6) were recruited from the skin clinic, National hospital of Sri Lanka, and age and gender matched- healthy controls (n=2) were also recruited. The sample size was restricted to 6 patients and 2 controls due to the technical difficulties encountered during the covid-19 pandemic. The sample size was, however, sufficient to calculate 6 data points for statistical analysis, however no statistical analysis was performed on the sample size which was a limitation in the study. Blood was collected from both patients and healthy controls. Total leukocytes were isolated using 6% Dextran sedimentation assay and phagocytes were separated after determining the viability. RNA was extracted from the isolated phagocytes, cDNA was synthesized immediately, and mRNA expressions were determined by RT-qPCR. Results showed that IL-6 levels were the highest among the cytokines tested in patients with psoriasis while IL-10 levels were the lowest. mRNA expression of TNF-α was 130-fold higher, IL-6 was 302- fold higher, IL-8 was 136.14 -fold higher and IL-10 was 5.2-fold higher in the patients compared to healthy controls. Accordingly, all four tested cytokine levels were high among the patients with psoriasis compared to healthy controls. Hence, increased inflammatory cytokine levels detected in patients may be contributing to the disease pathogenesis in psoriasis.

Keywords: psoriasis, cytokines, pro-inflammatory, anti-inflammatory, inflammation

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PP 03 (Abstract # 64)

Cross-reactivity of sera of patients allergic to venom of Sri Lankan ant species with *Apis dorsata* and *Vespa affinis* venom

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In Sri Lanka, anaphylaxis due to insects are caused by ant, bee and wasp stings. *In vitro* diagnosis of ant venom allergy is performed using whole body extracts due to the unavailability of purified ant venom allergens, leading to inaccuracies on account of cross-reactive carbohydrate determinants (CCDs). However, CCD-free bee and wasp venom components are available commercially for component resolved diagnosis of bee and wasp allergies. This study explores the cross-reactivity of venom from Sri Lankan ant species with components of *Apis dorsata* and *Vespa affinis* venom; and attempts to determine the utility of Western bee and wasp venom allergens in the diagnosis of ant venom allergies in Sri Lanka. Western blots were conducted using the sera of patients who developed anaphylaxis secondary to ant stings (n=25) and healthy controls (n=25), to identify cross-reactive allergens from *A. dorsata* and *V. affinis* venom. ImmunoCAP tests were then performed to quantify sIgE to rApi m 2, rApi m 5 of *A. mellifera* and rVes v 1, rVes v 5 of *Vespula vulgaris.* In the Western blots, cross-reactivity of patient sera was observed with dipeptidylpeptidase IV (96%), phospholipase A2 (92%), hyaluronidase (80%) of *A. dorsata* and dipeptidylpeptidase IV (96%), antigen 5 (88%) of *V. affinis.* Positive sIgE levels (>0.35 KUA/L) for rApi m 5 (75%), rVes v 5 (62.5%) and rApi m 2 (50%) and a combined positivity rate of 87.5% for rApi m 5 and rVes v 5 were seen in patient sera during ImmunoCAP testing. Considerable cross-reactivity with ant venom was seen in both *A. dorsata* and *V. affinis* venom, thus patients with ant venom allergy should be warned against exposure to bee and wasp stings. These findings also suggest that recombinant venom allergens of *A. mellifera* and *V. vulgaris* may be useful in ant venom allergy diagnostics in Sri Lanka.

Keywords: ant venom allergy, CCD, *Apis dorsata*, *Vespa affinis,* IgE cross-reactivity

Acknowledgements: This work was supported by Medical Research Institute (Grant No:32/2019) and Institute of Biochemistry, Molecular Biology and Biotechnology, University of Colombo.

PP 04 (Abstract # 11)

Assessment of A10398G polymorphism in the *MT-ND3* gene in sporadic breast cancer patients of Sinhalese ethnicity

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Breast cancer (BC) is the most common malignancy among women world-wide. Although most female breast cancers are sporadic, there are hardly any genetic biomarkers for its prediction. Mitochondria, the site of oxidative phosphorylation, constantly exposes its genome to intracellular reactive oxygen species. With evidence of the role of oxidative stress in carcinogenesis, mitochondrial genetic polymorphisms have been implicated in the susceptibility to various cancers including breast cancer. A10398G polymorphism in the *MT-ND3* gene has been previously studied in relation to breast cancer in several populations, but the findings have remained inconsistent. Some studies showed that the A allele at this locus confers increased risk while others showed the opposite or lack of an effect. A10398G variant, causes an amino acid substitution from threonine to alanine, within the mitochondrial respiratory chain complex I (RCC-1) subunit, NADH-ubiquinone oxidoreductase chain 3. We studied 60 pairs of Sinhalese women with sporadic breast cancer and healthy women matched for age, body mass index and menopausal status to ascertain possible association of A10398G variant with BC. Total genomic DNA extracted from peripheral venous blood was sequenced by Next Generation Sequencing (30 pairs) and by Sanger sequencing (30 pairs) of the *MT-ND3* gene. Within our cohort, the prevalence of the 10398A reference allele and the alternate allele were similar between the patients and the controls (10398A: patients=41.66%, controls=41.66%: 10398G; patients=58.33%, controls=58.33%) precluding a role for either allele in breast carcinogenesis. These results are consistent with previous observations in South Indian, Han-Chinese and Malaysian BC patients, but differs from observations in several other populations. SIFT/Poly-Phen2 servers predicted the polymorphism to be non-deleterious. Further, *in silico* modeling of the A10398G substitution indicated no significant changes in the protein structure (RMSD 0.445) or its interactions with other subunits of the RCC-1 supporting the observed frequency and non-deleterious nature of the polymorphism. Thus, A10398G polymorphism in the *MT-ND3* gene is unlikely to play a significant role in the development of sporadic breast cancer in women of Sinhalese ethnicity.

Keywords: *MT-ND3*, A10398G, sporadic breast cancer, Sinhalese, mt-DNA

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PP 05 (Abstract # 32)

Genomic surveillance of SARS-CoV-2 virus among infected people in Sri Lanka

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Whole-genome sequencing is used during outbreak situations for pathogen detection and characterization, mutation analysis, and transmission chain tracking. During our study, whole-genome sequencing was carried out on 9 samples from SARS CoV-2 positive patients. Nasopharyngeal swabs were collected in viral transport media from 53 SARS CoV-2 suspected patients who reported to Colombo North Teaching Hospital in August, 2021. Viral RNA was extracted from the swab using the QIAamp Viral RNA Mini kit. E-gen RT-PCR was carried out to determine the threshold cycle (CT) value of the samples. SARS CoV-2 viral genomes were amplified in samples with CT values between 8 and 13 using Midnight RT-PCR Expansion kit. Two 1200 bp multiplexed amplicon sets were fragmented and barcoded using the rapid barcoding SQK-RBK110.96 kit. The pooled DNA library was sequenced using SpotON flow cell on MinION Mk1C sequencing device. Real-time basecalling and demultiplexing were carried out using FAST basecalling model by MinKnow software. Genome assembly and variant calling of demultiplexed reads were performed following the ARTIC bioinformatics pipeline on the EPI2ME platform. Reads were filtered to a minimum 150 bp and maximum 1200 bp lengths. All 9 samples were identified as B.1.617.2 variant of SARS-CoV-2 and 7 samples out of 9, were assigned to AY.28 sub-lineage. AY.28 sub-lineage was first reported in Sri Lanka, and has the highest prevalence in Sri Lanka, accounting for 41% of total cases reported. Apart from the characteristic L452R mutation of delta variant, T19R, G142D, R158G, A222V, T478K, D614G, P681R, A701S, D950N, A1078S spike protein amino acid substitutions and E156- and F157- deletions were identified in all the samples. Continuous surveillance of the SARS-CoV-2 genome will be necessary to monitor new mutations and the evolution of the virus. All sequence data have been submitted to GISAID database.

Keywords: SARS CoV-2 whole genome sequencing, genomic surveillance, nanopore sequencing

Acknowledgements: This study was supported by Robert Koch Institute through the GHPP funded by the German Federal Ministry of Health.

PP 06 (Abstract # 42)

Association of selected genetic variants in *CBS* gene with clinicopathological characteristics in a cohort of children with Homocystinuria in Sri Lanka

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Homocystinuria, a rare recessive inherited disease, is characterised by an abnormal accumulation of homocysteine and its metabolites in blood and urine. It causes various severe complications in individuals, such as an increased risk of myocardial infarction, stroke, neurodegenerative diseases, pregnancy complications, mental retardation, ectopia lentis, myopia, glaucoma, osteoporosis, and thromboembolism, which are the major causes of morbidity and mortality in untreated CBS deficient patients. Mutations in the *Cystathionine β-synthase (CBS)* gene interrupts the production of the Cystathionine *β*-synthase enzyme, preventing homocysteine from being metabolised, leading to its accumulation. Therefore, detection and treatment in the early stages of the condition are important in preventing this condition from becoming life-threatening. This study was carried out to correlate the identified two variants in the *CBS* gene, c.19 del and c.833T>C, in individuals with the clinical characteristics of Homocystinuria. Blood samples from eight children who were confirmed to have CBS deficiency were collected, and a mutation analysis was performed. According to the results, out of 8 patients, none had c.833T>C polymorphism, but four patients have the c.19del mutation in the *CBS* gene. According to the results and gathered data, all the children have symptoms more or less similar to those associated with homocystinuria, where four children, who have c.19 del in homozygous condition had comparatively severe symptoms than the other patients. These patients presented wit severe clinical symptoms such as ectopia lentis, myopia, glaucoma, visual impairment, learning difficulties, marfanoid features and personality changes, in addition to having elevated total plasma homocysteine and methionine levels. However, further studies are needed with a larger cohort, since the current sample size is insufficient to conclude the outcome. Furthermore, it is important to study the correlation of both variants with the occurrence of the disease and its symptoms.

Keywords*:* homocystinuria, cystathionine β-synthase, mutation

Acknowledgements: This work was supported by the Institute of Biochemistry, Molecular Biology and Biotechnology and constituted part of MSc studies of Samarasinghe N.

PP 07 (Abstract # 43)

Association of selected genetic variants in the *MTHFR* gene and clinicopathological characteristics in a cohort of children with homocystinuria in Sri Lanka

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Homocystinuria, an inborn error of metabolism, is a rare autosomal recessive inherited disorder commonly detected in infants and children. Mutations in genes associated with homocysteine metabolism such as *Methylenetetrahydrofolate reductase (MTHFR),* or a nutritional deficiency of one or more vitamins involved in homocysteine metabolism (Vit B6, B12, B9) leads to the metabolic disruption and elevated plasma homocysteine levels seen in homocystinuria. This condition potentially has systemic effects, therefore, children with homocystinuria may develop several anomalies. For instance, they may present with ocular abnormalities such as ectopia lentis, myopia and glaucoma, skeletal abnormalities with marfanoid features, cardiovascular diseases such as thromboembolism, neurological disorders and developmental delays. This study aimed to determine the association of the variants c.665C>T (p.Ala222Val) and c.1286A>C (p.Glu429Ala) of the *MTHFR* gene with the reported clinicopathological characteristics of children with homocystinuria. Blood samples (N=8) were collected from a cohort of clinically confirmed children with homocystinuria in the Lady Ridgeway Hospital, Colombo and were analyzed for the possible variants. Seven out of eight children had the heterozygous condition for the A1286C variant, and one child had the heterozygous condition for the C665T variant. As per the clinical observations, all the children had high homocysteine levels and rather similar symptoms associated with homocystinuria. However, four children had relatively severe personality changes and neurodegenerative diseases in addition to the common symptoms associated with the disease. Furthermore, two children who were siblings had different heterozygous conditions of the *MTHFR* gene but presented with considerably similar symptoms. Thus, it is likely that other socio-demographic factors may also affect this condition. However, further studies in larger populations are necessary to gain a better understanding of the correlation between the identified variants and the clinicopathological characteristics seen in children with homocystinuria in Sri Lanka.

Keywords: homocystinuria, *Methylenetetrahydrofolate reductase,* variants

Acknowledgements: This work was supported by the Institute of Biochemistry, Molecular Biology and Biotechnology and constituted as a part of MSc. studies of Mahaliyanage D.

PP 08 (Abstract # 52)

Verification of the presence of mesenchymal stem cells in primary human endometrial cell

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Mesenchymal stem cells (MSC) are multipotent stem cells with high self-renewal and differentiation capacity. Isolation of these cells are usually carried out by different sources such as bone marrow, adipose tissue, umbilical cord and endometrium. Human endometrial stromal cells that are involved with cyclic regeneration processes have been identified as one of the rich sources of multipotent MSC and these cells are termed as endometrial MSC (eMSC). The expression of two vital cell membrane markers; CD146 and PDGFRβ has been considered as one of the verification tools to confirm the presence of eMSC in mixed cultures. Objective of the present study is to verify the presence of eMSC in primary human endometrial cultures by CD146 and PDGFRβ amplification. Primary endometrial cultures were established by obtaining endometrial biopsy samples from voluntary healthy women between 30-40 years at the proliferative stage of their menstrual cycle. Cells were continuously passaged in DMEM/F12 supplemented with 10% v/v FBS and 2% v/v penicillin/streptomycin at 5% humidified CO_2 incubator until uniform eMSC clonal expression was achieved. At the end of the third passage, CD146 and PDGFRβ and GAPDH genes were amplified using DNA extracted from eMSC. PCR conditions were optimized for clearly visible PCR amplicon for each targets; CD146 F, 5'-TGGTGCTCACCATCATCTCC-3'and R, 5'-CACCTTCCATCGGATCTCGTAA-3' (95°C for 2 minutes, 60°C for 30 seconds and 72°C for 5 minutes), PDGFRβ F, 5'-AGCATACCCGGCCTCAAC-3' and R, 5'-CCACACCTTCCTCTCCTTGAA-3'(59°C for 30 seconds and 72°C for 5 minutes), GAPDH F, 5-CATGGCACCGTCAAGGCTGAGA-3'and R, 5-CCATGGTGGTGAAGAGCCAGT-3'(60°C for 30 seconds and 72°C for 5 minutes). Amplified products were separated in 2% w/v agarose gels and visualized after staining with ethidium bromide. The presence of PCR amplicons for respective targets confirmed the presence of eMSC in mixed culture derived from primary endometrial cultures.

Key Words: endometrial mesenchymal stem cells, CD146, PDGFRβ, GAPDH

Acknowledgements: This work was supported by university research grant (ASP/01/RE/SCI/2021/19).

PP 09 (Abstract # 62)

Analysis on the structural genomic rearrangements in major cancers

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The Cancer Genome: a sequenced nucleotide profile of DNA and RNA in cancer cells often used to understand the type of cancer in order to determine its therapeutic interventions. The Cancer Genome Atlas (TCGA) is one of the important databases created using the latest modern sequencing technology to identify somatic variations in the cancer genome. Data from COSMIC (Catalogue of Somatic Mutations in Cancer) was used to analyze the relationship between types of mutation and twelve major cancers. Chromosome 1 showed the highest rearrangement density, and most of the cancers in humans occur due to intra-chromosomal structural changes with a non-inverted orientation. Inter-chromosomal deletion mutations were seen in all the primary sites except urinary tract. The prostate gland acts as the primary site for most genomic rearrangements while the upper aerodigestive tract contributes less.

Keywords: COSMIC, gene mutations, mutation density, cancer genome

Withdrawn

PP 10 (Abstract # 70)

Characterisation of complete *GH1* gene deletions discerned in two children with isolated growth hormone deficiency

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Growth hormone deficiency, a disorder of inadequate secretion of growth hormone (GH) from the anterior pituitary gland, leads to short stature. The most common genetic causes of isolated growth hormone deficiency (IGHD) are pathogenic mutations of the *GHRHR* (GH releasing hormone receptor) or *GH1* gene or deletions of the *GH1* gene. Previous studies from our group identified two IGHD children with two different types of *GH1* deletions (6.7 kb and 7.0 kb). Here we report the characterization of these two *GH1* gene deletions. DNA from the probands (Child A & Child B) and controls were amplified using polymerase chain reaction (PCR). Several sets of primers were designed to specifically anneal to the *GH1* gene and its flanking regions. They were designed to avoid amplifications of the paralogous genes. Rough locations of the breakpoints were discerned using different combinations of forward and reverse primers to amplify DNA by PCR. Sanger sequencing was carried out with selected primers to identify exact location of both types of deletions. The deleted segment in Child A is 6616 bp in length and the breakpoints are restricted within the 508 bp repeat located in homologous segments upstream and downstream of the *GH1* gene. The deleted segment includes the *GH1* gene and one of the 508 bp repeats. The deleted segment in Child B is 7325 bp in length with its breakpoints are restricted within a 15 bp repeat located upstream and downstream of the *GH1* gene. The deleted segment includes the *GH1* gene and one of the 15 bp repeats. In this study, endpoints of gross *GH1* gene deletions identified in two children biochemically confirmed to have IGHD have been characterized.

Keywords: GH1, IGHD, PCR, growth hormone, deletion

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PP 11 (Abstract # 21)

Isolation and molecular identification of some selected fungi with lignin degradation activity

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Lignin biodegradation plays a significant role in the global carbon cycle and certain fungi produce ligninolytic enzymes including laccase, lignin peroxidase and manganese peroxidase. The aim of this study was to isolate and identify fungi with lignin degradation activity. Degrading ligneous plant materials were collected with fungal fruiting bodies and cut in to ~0.5 mm^2 pieces, surface sterilized and inoculated on Potato Dextrose Agar (PDA) supplemented with guaiacol 0.04 % and chloramphenicol 0.03 % (w/v). Pure cultures of those isolates were further tested. Laccase activity was tested by guaiacol colour culture screening, guaiacol oxidation assay and 2,20-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) oxidation assay. Isolate number 2 gave the highest value of 21.0417 $\mu mol.min^{-1}$ and 2.2593 $\mu mol.min^{-1}$ for guaiacol and ABTS oxidation assays respectively. All tested fungal isolates were positive for all laccase assays. Lignin peroxidase activity was tested by methyl catechol assay and veratryl alcohol oxidation assay. Manganese peroxidase activity was tested by methylene blue reaction assay and manganese sulphate oxidation assay. The peroxidase activities were observed only after the concentration of proteins by ammonium sulphate precipitation, due to the low level of peroxidase enzymes. The more promising ligninolytic enzyme producers were subjected to molecular identification. DNA was extracted from the isolates and Internal Transcribed Spacer region of nuclear ribosomal RNA (rRNA) gene was amplified using ITS 1 and ITS 4 primers. The amplicons were bidirectionally sequenced and the resultant sequences were searched over GenBank database and according to the highest similarity all isolates were identified as *Trichoderma* species. Then their sequences were deposited in the GenBank database. Accordingly, the isolate number 2, 9-Brown and 36 were identified as *Trichoderma asperellum*, *Trichoderma lentiforme* and *Trichoderma asperellum* respectively and corresponding GenBank accession numbers are MZ602150, MZ602151 and MZ603114. Those Trichoderma isolates are prominent laccase enzyme producers and also exhibited low peroxidase activities.

Keywords: biodegradation, ligninolytic enzymes, laccase, lignin peroxidase, manganese peroxidase

PP 12 (Abstract # 22)

Genome-wide analysis of *GATA* gene family in angiosperms

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GATA transcription factors (TFs) contain a highly conserved type-IV zinc-finger (Znf) motif ($CX_2CX_{17-20}CX_2C$) followed by a basic region. In plants, these TFs participate in regulating diverse developmental processes and stress responses. However, no information is currently available on the *GATA* gene family across angiosperms. A comprehensive study was conducted to explore this gene family in 23 angiosperm genomes representing the major angiosperm lineages, basal angiosperms, monocots and eudicots. A total of 706 GATA TFs were identified, which were predominately localized to the nucleus. These proteins were phylogenetically clustered into five distinct subfamilies (I to V); five subclusters were observed within subfamily I (I-a to I-e). The majority of GATA factors of subfamilies I, II and IV consisted of a typical $CX_2CX_{18}CX_2C$ Znf loop in the GATA domain whereas subfamilies III and subfamily V contained a $CX_2CX_{20}CX_2C$ Znf loop in the GATA domain. Moreover, the majority of GATAs in subfamily III contained CCT and TIFY domains, subfamily IV contained ASX homology domain, and subfamily V contained MULE transpose, FAR1 DNA-binding and SWIM Znf domains. The analysis of chromosomal locations of *GATA* genes revealed that they are randomly distributed on chromosomes. The majority of *GATA* genes in subfamilies I and II contained two to three exons, subfamily III contained seven to ten exons, subfamily IV contained eight exons and subfamily V contained four to five exons. *In silico* promoter analysis suggested that *GATA* genes shared several *cis*-acting regulatory elements related to plant growth and development, metabolic regulation, hormone responsiveness, environmental stress-responsiveness and light responsiveness. Interestingly, protein-protein interaction analysis showed that GATA members of subfamily III are more likely to interact with other GATA members. Taken together, the findings of the present study provide an insight into the future functional genomics studies of *GATA* gene family in economically important crops.

Keywords: GATA transcription factor, angiosperms, phylogenetics, protein-protein interactions

Withdrawn

PP 13 (Abstract # 44)

Effect of *Exobasidium vexans* infection in tea (*Camellia sinensis.* (L.) O. Kuntze) on the expression of flavonoid biosynthetic enzymes and biosynthesis of flavonoids

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Tea (*Camellia sinensis.* (L.) O. Kuntze) is an economically important leaf crop, therefore, pathogen infections on tea leaves are a major concern in the tea industry. Blister blight infection by the fungus *E. vexans* is one such disease. During the infection, flavonoids and other phenolic compounds accumulate at a higher concentration as a defence mechanism. The objectives of this study were to determine the effect of *E. vexans* infection on the expression of selected flavonoid biosynthetic enzymes in tea *i.e*., Dihydroflavonol 4-reductase (DFR), Leucoanthocyanidin reductase (LAR), and Anthocyanidin reductase (ANR), and the biosynthesis of flavonoids using real time quantitative PCR and High-Performance Liquid Chromatography (HPLC) methods respectively. HPLC Analysis was carried out according to International Organization for Standardization method (ISO) 14502-2: 2005 procedure with some modifications. Extraction of RNA from lyophilized tea samples from healthy and infected tea leaves *i.e*., Healthy leaves (HL), Translucent (TL), Mature blister stage 1 (MB1), Mature blister stage 2 (MB2) was carried out using TRIzol reagent-based method, and cDNA was synthesized. Real time qPCR experiments were performed with gene-specific primers for *dfr, lar, anr* genes using QuantiNova SYBR Green mix (Qiagen) and CFX96 (BioRad) Real-Time PCR System to measure the transcription levels of the genes. The 18s rRNA gene was used as a normalization control. Real time qPCR results revealed that *dfr, lar, anr* genes were up-regulated showing the fold change as 7.08, 6.34, and 1.68 respectively in the initial diseased stage and down-regulated in the latter part of the disease, showing fold change as 0.84 and 0.06 for *dfr* and *anr* respectively compared to the healthy sample. HPLC data also revealed that increased accumulation of proanthocyanins in the final stage (MB2) of the disease showed a value of 1.1894 mg/g. This could be attributed to the defence response of the flavonoid biosynthesis pathway.

Keywords: *Camellia sinensis*, *Exobasidium vexans*, flavonoids, blister blight disease, proanthocyanidins

Acknowledgements: This work constitutes a part of MSc studies of Edirisinghe KAMJ.

PP 14 (Abstract # 45)

Development of DNA based accurate identification method for agarwood produced by endemic threatened *Gyrinops walla*

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Gyrinops walla (Walla Patta) is an Agarwood producing endemic plant in Sri Lanka, which has a high demand in the world aroma market for its fragrance. It is the only Agarwood producing plant available in the natural habitat of Sri Lanka. Due to its high economic value, large-scale smuggling of agarwood has been practiced for a long time. Agarwood smugglers are taking advantage of the unavailability of accurate agarwood identification methods. Prevention of illegal agarwood trade will facilitate the conservation of this valuable tree *spps*. DNA-based rapid and accurate agarwood identification method will help to prevent the illegal agarwood trade in Sri Lanka and will eventually lead to conserve the *Gyrinops walla*. In the present study, two chloroplast DNA regions (matK and trnL-trnF) and one genomic DNA (ITS) region of *G.walla* were amplified and sequenced. The obtained sequences were compared with the sequences of the *Aquilaria* species commercially cultivated in Sri Lanka. A total of 53 variable regions were observed, however, a high number of single nucleotide polymorphisms were identified in the ITS region in comparison to the other two barcode region. A total of seven molecular markers were designed, of which five were designed for the variable regions of the ITS and two markers for the variable regions of matK and TrnL-trnF regions. An *in-silico* PCR performed by fastPCRtool predicted the specificity of the designed molecular markers. Expected product sizes were from 88bp to 239bp. However, it is essential to conduct wet-lab experiments to ensure the usability of newly designed molecular markers to differentiate *G.walla* from the other *Aquilaria* species that are known to produce agarwood. Hence, these newly designed molecular markers for *G.walla* may be a valuable resource to prevent illegal trafficking of agarwood from Sri Lanka in the future.

Keywords: *Gyrinops walla*; conservation; prevention of illegal trafficking; molecular markers

PP 15 (Abstract # 34)

Comparison of rat immune responses to two pathogenic *Leptospira* serovars prevalent in Sri Lanka

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Leptospirosis is a zoonotic disease caused by spirochaetes of genus *Leptospira*, distributed worldwide, but endemic to Southeast Asia. Identification of immunogen profiles of pathogenic *Leptospira* serovars are important in establishing immunodiagnostics for leptospirosis. This study aimed to identify and compare rat immune responses against two pathogenic *Leptospira* serovars prevalent in Sri Lanka with their immunogen profiles. Sonicated antigen preparations (2 $x10^7$/dose) of two *Leptospira* serovars*;* serovar Bakeri and Pyrogenes, were used to immunize rats with Freund's complete and incomplete adjuvant. Rat sera were obtained by weekly bleeds, and the immune response was assessed using an In-house ELISA. Immune serum samples with highest titers were used for immunoblotting to identify the immunogen profiles of the two pathogenic *Leptospira* serovars. Rat IgM response against serovar Bakeri compared to serovar Pyrogenes was higher from Day 07 onwards except on Day 35 and 56, as reflected by both IgM titer and OD at 1:100 serum dilution. Similarly, the rat IgG response against serovar Bakeri compared to serovar Pyrogenes was significantly higher from Day 07 to 63 ($p<0.05$) and consistently increased up to 12,800 in the Bakeri titer compared to 1,600 in the Pyrogenes titer. Immunoblotting with homologous rat antisera showed immunoreactivity with 6 and 4 antigens in Pyrogenes and Bakeri respectively ranging from MW 15 -156 kDa. The identified reactive antigens were subjected to western blotting with heterologous anti-sera and the results showed that two antigens were cross reactive in both serovars. The observed immune responses, immunogenic antigen profiles and immune cross reactivity of the antigens between the two pathogenic *Leptospira* serovar*;* serovar Bakeri and Pyrogenes prevalent in Sri Lanka will be useful in considering and selecting target antigens for the development of immunodiagnostics.

Key words: *Leptospira,* serovars, antigen profile, immunoreactivity, immunodiagnostics

Acknowledgements: This work is supported by International Centre for Genetic Engineering and Biotechnology (ICGEB grant CRP/LKA 17-01).

PP 16 (Abstract # 6)

Effect of aqueous extracts of cinnamon bark on hyperglycaemia in diabetes induced Wistar rat models

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Diabetes mellitus is considered as the epidemic of the century. Although effective treatments are available, novel treatment modalities are being explored. The blood glucose lowering ability of *Cinnamomum verum* in diabetes induced Wistar rats was determined in this study. Ethical clearance was obtained for this study. Freeze-dried cinnamon bark aqueous extracts were prepared. Diabetes was induced with Streptozotocin at a dose of 40 mg/kg via an intraperitoneal injection. Diabetes rats were grouped (6 rats/group) to treat with cinnamon, and metformin. Cinnamon and metformin treated arms received 20 mg/kg/day cinnamon extract and 200 mg/kg/day metformin via oral-gavage for 42 days. Fasting blood sugar (FBS) in mg/dL was measured baseline and 2-weeks' intervals by tail vein blood and finally by cardiac puncture. Aminotransferase (AST), alanine-aminotransferase (ALT), alkaline-phosphatase (ALP) in U/L, and serum-creatinine in mg/dL were performed. Friedman and Krushkal-Wallis tests were used for statistical analysis using SPSS. In cinnamon-treated arm, median FBS (IQR) at baseline and 4-weeks after the treatment were 309.78 (255.54 - 352.24) and 119.13 (105.06-147.34) ($p = 0.03$). In the metformin-treated arm, median of FBS (IQR) at baseline and 4-weeks after the treatment were 224.45 (215.7-302.32) and 206.20 (159.51-269.94); ($p = 0.4$). The median (IQR) of reduction of FBS during the treatment in cinnamon and metformin treated arms were 169.06 (150.25-216.42) and 18.16 (-48.57-137.14) ($P = 0.344$). Median (IQR) of AST, ALT, ALP and creatinine of cinnamon-treated arm after 42 days were 50.63 (30.85-54.13), 21.83 (13.97-29.1), 92.82 (36.76-117.63) and 1.24 (1.12-1.29) respectively while in the metformin-treated arm, values were 67.51 (59.36-77.12), 20.95 (18.33-34.92), 19.75 (15.16-25.73) and 0.53 (0.45-0.61) respectively. There were no significant difference of liver or renal functions between two arms. Therefore, it was concluded that cinnamon bark aqueous extracts improve hyperglycaemia compared to metformin without causing adverse effects to liver and kidney.

Keywords: *Cinnamomum verum*, diabetes mellitus, dietary supplements, glycemic control

Acknowledgements: This work was supported by AHEAD-DOR05 grant.

PP 17 (Abstract # 24)

Protein-ligand site-specific docking for Plasmepsin-II Malaria receptor and identification of ligands and their binding sites

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Plasmodium species causes severe malarial infections, affecting approximately 229 million people in 2019. While several effective anti-malarial treatments exist, resistance to these treatments has increased the need for developing new drug targets. In this study, protein-ligand docking aimed to identify the best complex, and potential ligand binding sites. Malarial protein, Plasmepsin-II (ID: 1LF4) was retrieved from RCSB-PDB. Meanwhile, 3D structures of the phytochemicals were retrieved from PubChem. Active sites of the protein were identified by CASTp. Protein-ligand site-specific docking was performed using Autodock 4.2.6. Grid parameters were set by covering the area with the active sites of the receptor (X=98,Y=88,Z=70,grid_spacing=0.375). Lamarckian GA was used and the docking parameters were set as 50 GA runs and 300 population size. The docking results were analyzed by their lowest binding energy from the RMSD table. The best pose of the phytochemicals were visualized by BIOVIA Discovery Studio and H-bond interactions were determined using LigPlot+. ADMET properties of the phytochemicals were analyzed by SwissADME. By applying thermodynamics, lower binding energy indicates a more stable complex. Thereby, Serpentine, Tehranolide, Aloin, Myricetin, Citral exhibited lowest binding energies (-8.16,-6.7,-6.42,-5.28,-5.17 kcal/mol respectively). This identifies Serpentine as a stable complex. Serpentine showed an inhibition constant (Ki) of 1.04 nM with one H-bond. Low Ki and the presence of a hydrogen bond indicates greater binding affinity and stability. GLY36, SER37, MET75, TYR77, VAL78, SER79, PHE111, TYR192 and GLY216 are potential ligand binding sites. The pharmacokinetics of Serpentine includes high gastrointestinal absorption and blood-brain barrier (BBB) permeability. Moreover, it accepts Lipinski's rule with no violation. These results confirm Serpentine as a potential ligand for 1LF4. Serpentine can be extracted from *Rauvolfia serpentine*, a perennial shrub belonging to Asian countries, including Sri Lanka. Therefore, Serpentine suggests suitable therapeutic interventions to treat Malaria. Further, validation and investigation using wet-lab experiments are required.

Keywords: Plasmepsin-II, Serpentine, site-specific docking, RMSD, binding energy

PP 18 (Abstract # 27)

Protein-ligand docking for the identification of therapeutic ligands against the Nipah virus attachment glycoprotein using AutoDock

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Nipah virus (NiV) infection caused by the BSL-4 zoonotic pathogen NiV; was identified as a blueprint priority disease by the WHO in 2018. It was first reported in Malaysia followed by sporadic outbreaks in Bangladesh and India. Natural reservoirs of the NiV are fruit bats of the *Pteropus* genus which are endemic to South and Southeast Asia. Zoonosis occurs through contaminated body fluids. NiV infection provokes febrile encephalitis and respiratory diseases associated with a fatality rate of ~70%. Currently, there are no specific drugs, therapies, or vaccines against this disease. In this study, protein-ligand docking was performed to identify therapeutic ligands against the NiV attachment glycoprotein (PDB ID: 2VSM) which is a virulent-factor mediating pathogenicity through host-cell adhesion. The blind-docking technique was utilized in the AutoDock 4.2.6. FDA-approved drugs for standardization and phytochemicals as novel therapeutics were chosen. ADMET properties such as physiochemistry, lipophilicity, water-solubility, pharmacokinetics, druglikeness, and medicinal-chemistry were analyzed using SwissADME to identify probable phytochemicals. Binding free energy (BE), inhibitory constant (Ki) and hydrogen interactions (HI) (acquired from BIOVIA/LIGPLOT^{+} v2.2) were the primary parameters analyzed. Lower BE which is proportional to the lower potential energy of the system demonstrated higher stability of a docked complex. Lower Ki represented the integrity of the ligand to inhibit the protein. Higher HI proportionated with higher resistance to bond breakage within the docked complex. The aptest ligands were found to be FDA-approved drugs; Tolvaptan (BE: -12.05kcal/mol, Ki: 1.48nM, HI: 6) and Conivaptan (BE: -10.94 kcal/mol, Ki: 9.52nM, HI: 1), phytochemicals; Neoandrographolide (BE: -7.97 kcal/mol, Ki: 1.45 µM, HI: 5) and Demethoxycurcumin (BE: -7.97kcal/mol, Ki: 1.43µM, HI: 5). Our findings suggest that phytochemicals extracted from plants endemic to South-Asia; *Andrographis paniculate* (Neoandrographolide) and *Curcuma longa* (Demethoxycurcumin) can be utilized as leads for antiviral drug development against NiV, as plant-based antivirals show less toxicity/adverse effects.

Keywords: Nipah virus, NiV attachment glycoprotein, AutoDock, blind docking, drug development

PP 19 (Abstract # 29)

Scientific investigation on Sri Lankan polyherbal drug ‘‘Neelagiri Padmana’’ for its antioxidant activity, polyphenol content and GC-MS analysis

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“Neelagiri Padmana” (NP) is a traditional polyherbal formulation used to treat abscesses, wounds and cancers based on Ola leave inscriptions by traditional medical practitioners in Sri Lanka. This study attempted to investigate antioxidant and bioactive phytochemicals to validate their usage in traditional medicine. Aqueous extracts from dried NP were prepared by a method similar to traditional “Kasaya” briefly refluxing followed by concentration. Then the aqueous extract was lyophilized. The total phenolic content of NP extracts was evaluated using the Folin-Ciocaltau assay and expressed as gallic acid equivalents (GAE) and a 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay was carried out to evaluate *in vitro* antioxidant capacity using ascorbic acid as the standard. Furthermore, GC-MS fingerprinting analysis was carried out using an ethanolic extract of NP to investigate the presence of the bioactive phytochemicals present. All the experiments were carried out in triplicates and a linear regression model was used to analyze the data. The aqueous extract of NP demonstrated a substantial amount of antioxidant activity (IC_{50} = 66.33 ppm) compared to ascorbic acid (IC_{50} = 33.71 ppm) and polyphenol content of 3.40 ± 0.24 GAE. Moreover, the GC-MS analysis of the ethanolic extract of NP shows the presence of propane-dioic acid, Azitidine-2-one derivatives, Carbamic acid, Butanoic acid, Alanyl glycine and a few other Phenol derivatives as major constituents. Thus, these results show the presence of high total phenolic content, and a higher DPPH radical scavenging activity compared to gallic acid and ascorbic acid respectively.

Keywords: Neelagiri Padmana, antioxidants, DPPH, polyphenol

PP 20 (Abstract # 36)

A molecular docking study revealed natural benzophenones and xanthones from *Garcinia zeylanica* as Wnt and Hedgehog pathway inhibitors in breast cancer stem cells

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The Cancer stem cell (CSC) hypothesis explains that CSCs are a rare stem cell population, found within malignant tumours, and may be linked to the multidrug resistance, recurrence, and metastasis seen in multiple cancers. Further, the dysregulation of Wnt and Hedgehog signalling pathways, and the aberrant activation of *β*-catenin effector and smoothened (SMO) transducer were evidenced in CSC survival. Thus, targeting these signalling pathways could be a better treatment strategy. We identified four compounds isolated from a plant endemic to Sri Lanka; *Garcinia zeylanica* that suppressed bCSC proliferation. However, their molecular targets have not been studied. This study investigates the molecular targets of the four compounds in Wnt and Hedgehog pathways using an *in-silico* setting. Structures of these compounds were drawn in ADM/ChemSketch and optimized with Avogadro. *β*-catenin and SMO proteins were prepared by extracting the chain-A using UCSF Chimera 1.8.1. Side-chains were replaced using the DOCKPrep protocol. Ligands were docked with proteins in AutoDock-Vina. The binding pose was analyzed using AutoDock-Vina, VEGA-ZZ, Pymol, and protein-ligand interaction profiler. Drug-likeness and ADMET properties were analyzed in FAFDrugs4 and admetSAR servers. Results indicated that nigrolineaxanthone-E, garcinol, and 14-deoxygarcinol hit desirable scores for *β*-catenin. Hotspot-A of *β*-catenin forms high-affinity interactions with TCF4 at Lys435, Arg469, Lys508, Arg515, and Glu571 and provide a sufficient binding pocket for small molecules. In *β*-catenin and Tcf4 interaction; Lys435 and Arg469 were blocked by nigrolineaxanthone-I and garcinol, whereas Arg515 was blocked only by 14-deoxygarcinol. 14-deoxygarcinol also blocked Arg469. Gerontoxanthone-I blocked SMO at Asp219 and Asp384 with −6.8 kcal/mol binding energy, in which Asn219, Asp384, Lys394, Arg400, Asp473, and Glu518 are the major interaction points. Drug-likeness analysis of the compounds satisfies Egan’s model and Veber’s rule. These findings suggest that the four lead compounds isolated from *Garcinia zeylanica* can be improved to produce agents that target CSCs.

Keywords: cancer stem cells, *β*-Catenin, SMO receptor, Wnt signaling pathway, Hedgehog signaling pathway, molecular docking

Acknowledgements: This work was supported by the National Research Council of Sri Lanka under Grant NRC-14-067.

PP 21 (Abstract # 55)

Effect of *Munronia pinnata* on function a changes of endothelial cells interacted with DENV-3

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Infection of endothelial cells (ECs) and their dysfunction has been implicated in the immunopathogenesis of the dengue virus (DENV), which lead to increased severity. Therefore, the therapeutic targeting of the endothelium may be an excellent treatment strategy. *Munronia pinnata* is a rare medicinal plant that is commonly used to treat fever in traditional systems of medicine in Sri Lanka. The objective of this study was to investigate the effect of the aqueous plant extract (APE) of *M. pinnata* on the interaction between DENV-3 and ECs. The effect of DENV-3 on the metabolic activity of ECs was evaluated by using MTT. The effect of APE of *M. pinnata* on the interaction between DENV-3 and ECs was assessed in three different ways to determine the potential of *M. pinnata* to protect the endothelial cells during a dengue infection; i) pre-treatment of DENV-3 with APE prior to exposure, ii) sequential treatment of ECs with DENV-3 followed by APE treatment and iii) sequential treatment of ECs with APE followed by DENV-3. A 49.8% reduction of EC viability was recorded following interaction with DENV-3 as opposed to that in the absence of DENV-3 ($p<0.001$). However, significant protection of ECs was observed at almost all concentrations of APE in our treatment strategies. Interestingly, increased protection was observed during the pre-treatment of DENV-3 with APE prior to its interaction with ECs (lowest $p=0.0003$), and the highest protection of EC was observed at 15.6 and 31.3 µg/mL of APE ($p<0.0001$). This study suggests that the APE of *M. pinnata* exhibits an antiviral effect against DENV-3 by protecting the metabolic activity of ECs. Further studies are needed to understand the underlying mechanisms of the direct inhibitory activity of *M. pinnata* against DENVs, and to characterize the active compounds.

Keywords: *Munronia pinnata*, dengue virus, endothelial cells, immunopathogenesis, cell proliferation assays

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PP 22 (Abstract # 67)

Phytochemicals Coated Silver Nanoparticles as Potential Vehicles for the Delivery of Plant Natural Products

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Most plant extracts used in traditional medicines possess inherent antimicrobial activity, and nanosizing them or incorporating them into nanostructures may further enhance their efficacy. In this study, silver nanoparticles (AgNPs) were synthesized using aqueous extracts of plants used in ayurvedic medicine to treat wounds: *Lannea coromandelica* (Indian ash tree, hik, Family: Anacardiaceae) and *Pothos scandens* (climbing aroid, pota wel, Family: Araceae). Stem bark of *L. coromandelica*, leaves and stems of *P. scandens* were dried and pulverized. *L. coromandelica* and *P. scandens* (10 g) were sonicated (44 kHz, 40 ºC, 30 min) separately, in H_2O. Different concentrations of the aqueous extracts (2.5, 5, 7.5 mg/mL) were each individually mixed with aqueous $AgNO_3$ to synthesize LC-AgNPs and PS-AgNPs. Several different conditions i.e., homogenization or magnetic stirring with exposure to UV light/sunlight/dark were employed and yields were optimized based on UV spectral data. The reduction of $AgNO_3$ by the phytochemicals were analyzed using UV−Vis spectra in the range of 200−600 nm. AgNPs were characterized using particle size analyzer and atomic force microscopy (AFM). The observed Z-average particle diameter was 200.2±1.0 nm with a polydispersity index (PDI) of 0.435 for LC-AgNPs with a zeta potential at –20.3±1.2 mV. The PS-AgNPs showed the Z-average particle diameter of 216.8±0.7 nm with PDI of 0.401 and a zeta potential at –20.2±0.7 mV. The Z-average particle diameter, PDI and zeta potential of uncoated silver nanoparticles (U-AgNPs) were 128.8±0.8 nm, 0.474 and –17.6±1.2 mV respectively. AFM revealed the presence of spherical LC-AgNPs and PS-AgNPs of the size ranges 100–300 nm and 200–400 nm respectively. The AFM images on U-AgNPs revealed the presence spherical nanoparticles in the 200–400 nm. This study revealed two novel methods of phytochemicals-assisted synthesis of AgNPs.

Keywords: natural products, medicinal plants, phytochemicals, nanoparticles

Acknowledgement: This work was supported by Faculty of Medicine, University of Ruhuna (Faculty Research Grant FoM/RG2021/04).

PP 23 (Abstract # 69)

Antioxidant, antibacterial, and antifungal activities of flowers of *Hibiscus spp*

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The Hibiscus plant (Family: Malvaceae) has many therapeutic properties, and is commonly used in the production of medicine, cosmetics, and food and beverages in some parts of the world; however, it is not used for many purposes in Sri Lanka. In this study, the antioxidant level, total phenolic content (TPC), and the antimicrobial and antifungal effects of eleven Hibiscus flower varieties available in Sri Lanka were investigated. The antioxidant level was determined by the DPPH method, while the total phenolic content was determined by the Folin-Ciocalteu method. The disc diffusion test was used to evaluate the antimicrobial activity of *Hibiscus sp.* against *Escherichia coli, Salmonella typhi, Staphylococcus aureus, Pseudomonas aeruginosa*. In addition, the antifungal activity of *Hibiscus sp.* was measured against *Candida albicans* using the same method. Among the Hibiscus varieties studied, *Hibiscus rosa-sinensis* showed the highest antioxidant activity (94.27%) while *Hibiscus schizopetalus* has the lowest antioxidant activity (91.38%). The IC_{50} value determined for Hibiscus flowers ranged from 764.873 ± 31.65 ppm (*Hibiscus rosa-sinensis*) to 3546.46 ± 537.4 ppm (*Hibiscus schizopetalus*) respectively. The highest and lowest total phenolic contents in Hibiscus flowers were reported as 3000.06 mg GAE /100g and 1195.45 mg GAE/100g in *Hibiscus rosa-sinensis* and *Hibiscus schizopetalus* respectively. The inhibition zone of *Hibiscus rosa-sinensis* against *Escherichia coli, Salmonella typhi, Staphylococcus aureus, Pseudomonas aeruginosa* were reported as 1.20 cm, 1.18 cm, 0.92 cm and 1.20 cm respectively, thus showing almost similar microbial activity against the selected bacterial pathogens. The highest antifungal activity against *Candida albicans* was observed in *Hibiscus rosa-sinensis* (1.30 cm) while the lowest inhibition zone was examined against *Hibiscus schizopetalus* (0.75). In conclusion, *Hibiscus rosa-sinensis* flower has shown promising biochemical activity, thus further studies are required to explore the possibility of using it for therapeutic purposes.

Keywords: *Hibiscus rosa-sinensis,* antioxidant, antimicrobial, antifungal, disc diffusion

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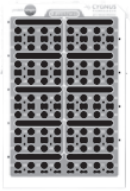


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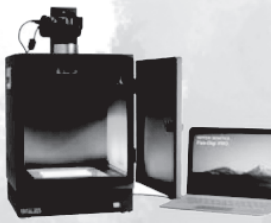


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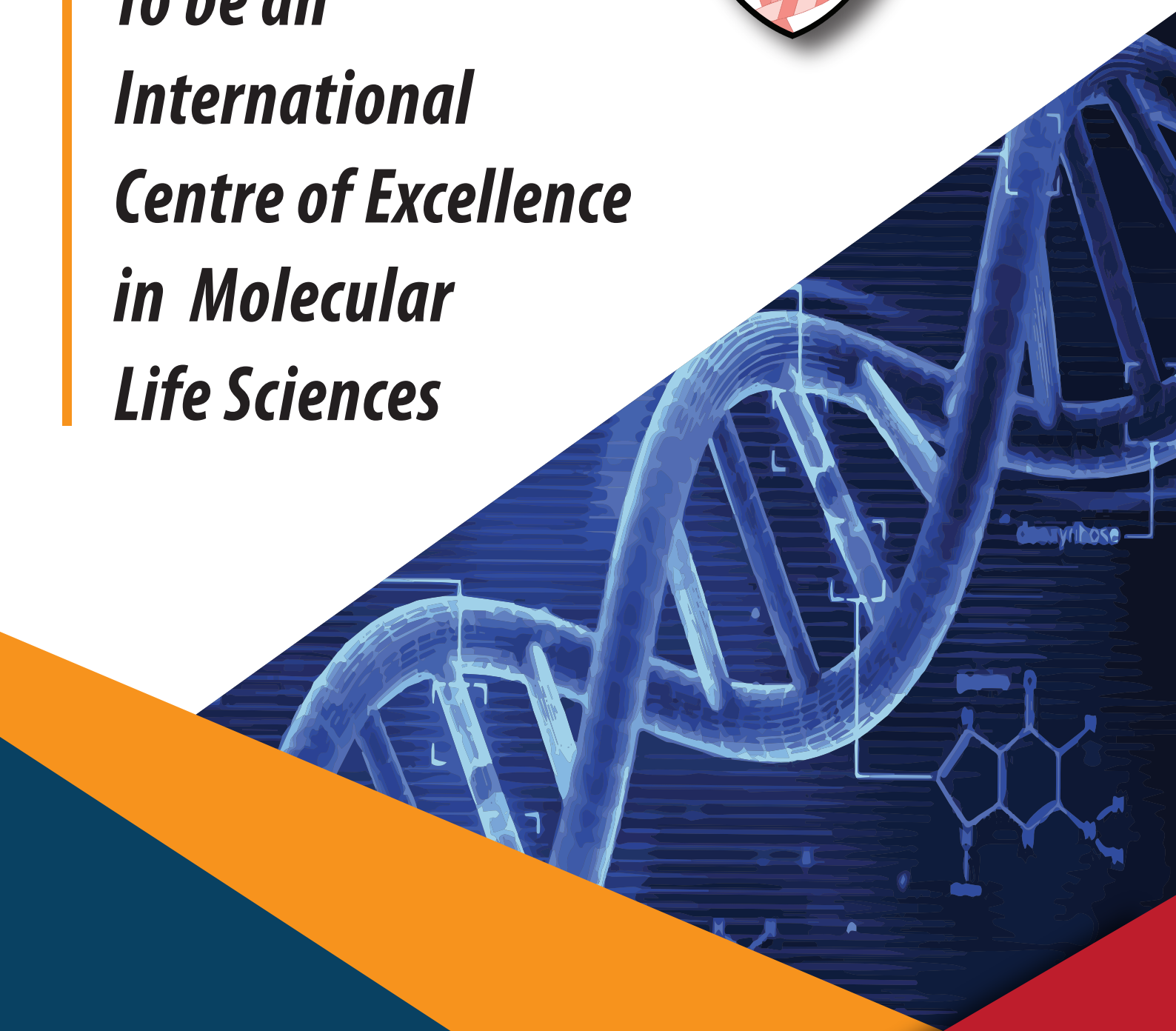

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