SCI SYNOPSIS

European Congress on

Human Genetics

November 06-07, 2023

Paris, France

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Conference Programme

Conference Programme

November 06-07, 2023, Millennium Hotel Paris Charles De Gaulle, Paris, France

Day 1, November 06, 2023

Meeting Hall - Room Bleriot

08:30-09:15	**Registrations**
09:15-09:30	**Introduction**

Keynote Presentations

09:30-10:15	**Jacques Pouysségur,** Institute of Research on Cancer and Aging in Nice (IRCAN), France

Title: Fermentative Glycolysis Controls Tumor Growth, Bacterial, Viral Infections and Immunity: Genetic Deconstruction and Therapeutic Perspectives

10:15-11:00	**Degen Zhuo,** BioTailor Inc, USA

Title: Hereditary Fusion Genes as the Dominant "Inherited" Genetic Factors Associated with Human Inheritances

Group Photo Session(11:00-11:10)

Networking & Refreshments @ Foyer (11:10-11:30)

Oral Presentations

Session Chair:	**Jacques Pouysségur,** Institute of Research on Cancer and Aging in Nice (IRCAN), France

Sessions: Bioinformatics in Genetics | Genetic Disorders | Biochemical Genetics | Cardiogenetics | Genetic Epidemiology | Epigenetics | Stem Cell Research and Gene Therapy | Gene Editing and Genetic Engineering | Cytogenetics | Population Genetics | Molecular Genetics | Immunogenetics

11:30-12:00	**Peter Kovermann,** Forschungszentrum Jülich GmbH, Germany

Title: Glutamate Transporter Missense Mutations Associated to Epileptic Encephalopathy Affect both, Transport and Channel functions

12:00-12:30	**Hasan Simsek,** Aksaray University, Turkey

Title: Beneficial Effects of Chrysin on Cadmium-Induced Nephrotoxicity in Rats: Modulating the levels of Nrf2/HO-1, RAGE/NLRP3, and Caspase-3/Bax/ Bcl-2 Signaling Pathways

12:30-13:00 **Arwa Khashkhusha**, University of Manchester, United Kingdom

Title: Thoracic and Abdominal Aortic Aneurysms: Exploring their Contrast and Genetic Associations

Lunch @ Restaurant (13:00-14:00)

14:00-14:30 **Karin EM Diderich,** Erasmus MC, Netherlands

Title: Challenges and Pragmatic Solutions in Pre-Test and Post-Test Genetic Counseling for Prenatal Exome Sequencing

14:30-15:00 **K.H.Mok,** Trinity College Dublin, Ireland

Title: Application of Novel AI-based Algorithms to Biobank Data: Uncovering of New Features and Linear Relationships

15:00-15:30 **Xianyang Liu,** Chongqing Medical University, China

Title: De Novo Missense Mutations in MPP2 Confer Increased Risk of Vogt-Koyanagi-Harada Disease by Trio-Based Whole Exome Sequencing

15:30-16:00 **Kareem Awad,** Ruprecht-Karls University of Heidelberg, Germany

Title: Hyperglycaemia Induces TGFβ1-Differential Gene Expression in Primary Human Immune Cells

Networking & Refreshments @ Foyer (16.00-16.30)

16:30-17:00 **Milica Komnenić Radovanović,** Medical Universitz of Belgrade, Serbia

Title: Undifferentiated Round Cell Sarcoma in Infant with both CIC and EWSR1 Aberration: Case Report

17:00-17:30 **Arwa Khashkhusha,** University of Manchester, United Kingdom

Title: Deciphering Ethnic Disparities in BC Genomics: Unmasking Driver Genes to Bridge the Oncogenic Divide

Day 1 Concludes followed by Awards Ceremony

Day 2, November 7, 2023

Meeting Hall - Room Bleriot

Keynote Presentations

9.00 - 9.45 — **Milica Vucetic,** Centre Scientifique de Monaco, France

Title: Genetic Dissection of Anti-Ferroptotic Axis Reveals Irreplaceable Factors for Cancer Cell Survival

9.45 - 10.30 — **Mohammad Kaleem Ahmad,** King George's Medical University, India

Title: Deciphering Non-Invasive Biomarker Potential of Circulating microRNA in Prostate Cancer

Networking & Refreshments @ Foyer (10:30-11:00)

Oral Presentations

Session Chair: **Mohammad Kaleem Ahmad,** King George's Medical University, India

Session Co-Chair **Vijay Gupta,** Qatar Biomedical Research Institute, Qatar

Sessions: Cancer Genomics | Genetic Medicine | Genome Integrity | Pharmacogenomics and Toxicogenomics | Nutrigenetics & Nutrigenomics | Genetic Vaccines | Proteomics, Genomics and Metabolomics | Diagnosis and Prognosis of Inborn Disorders | Phylogenetics | Clinical Genetics | Genomic Ethics | Mitochondrial Genetics

11.00 - 11.30 — **Vijay Gupta,** Qatar Biomedical Research Institute, Qatar

Title: Genome Sequencing from 50 Autism Trios Identified Novel Candidate Genes with Mixed Inheritance Pattern in the Qatari Population

11.30 - 12.00 — **Subhanullah Kahn,** Chinese Academy of Sciences, China

Title: A Comprehensive Review on the Roles of Metals Mediating Insect–Microbial Pathogen Interactions

Poster Presentations

12.00 - 12.15 — **Zilton Vasconcelos,** National Institute of Women's Health Child and Adolescent Fernandes Figueira, Brazil

Title: Correlations Between Genotype and Phenotype in Hereditary Hyperferritinemia-Cataract Syndrome: An Analysis of Three Brazilian Family Case Series

12.15 - 12.30 **Chandra Devi,** Banaras Hindu University, India

Title: Genetic Variability in Autosomal Dominant Polycystic Kidney Disease: Input from High Throughput Genome Analysis

12.30 - 12.45 **Abeer Zakariyah**, University Of Jeddah, Saudi Arabia and **Sultan M. Altouri,** King Fahad Armed Forces Hospital, Saudi Arabia

Title: A Case Representation of AIP with Pathogenic Mutation in HMBS gene

12.45 - 13.00 **Prashant Ranjan,** Banaras Hindu University, India

Title: Paving the Way: Progress in Tooth Agenesis Diagnostics and Therapeutic Solutions

Lunch @ Restaurant (13:00-14:00)

Video Presentations

VP001 **Roxana Villanueva Macedo,** Bioscience Research Laboratory, Los Altos University Center, Mexico

Title: Inflammatory Determinants and Associated Morbidity in Hemodialysis Patients

VP002 **Luidmila Lazarenko,** Saint Petersburg Pasteur Institute, Russia

Title: New Mutation in SERPING1 gene c. 860 T>G is a Associated with C 1-INH -HAE Type 1

Day 2 Concludes followed by Panel Discussion - Awards & Closing Ceremony

Virtual Programme

November 06, 2023

Day 1 November 06, 2023 GMT (London Time: 10.00 - 16.25)

Oral Presentations

10.00 - 10.25 — **Eleni Petsalaki,** University of Crete, Greece

Title: A Novel Mechanism Promotes Actin Patch Formation to Prevent Chromatin Bridge Breakage in Cytokinesis

10.25 - 10.50 — **Niharika Lal,** Metro College of Health Sciences and Research, India

Title: Alzheimer Disease: Is disease Related to Genes

10.50 - 11.15 — **Muhammad Adnan Younis,** Shenzhen University, China

Title: Synthesis, Biological and Molecular Docking Studies of Pyrimidine-derived Bioactive Schiff Bases

11.15 - 11.40 — **Sara Minaeian,** Iran university of medical sciences, Tehran Iran

Title: Assessment of Gut Bacterial Profile in Diabetic Patients Undergoing Bariatric Surgeries Using Quantitative PCR

11.40 - 12.05 — **Hafiza Farhat,** Gomal University D.I Khan, Pakistan

Title: Evaluation of Antibacterial Potential of Penicillium Species and Gc-Ms Metabolic Profiling of Penicillium Nigricans

12.05 - 12.30 — **Tehreem Iman,** Government College University Faisalabad, Pakistan

Title: Chitosan-Coated Nanoparticles of Calotropis Procera Escalate Functions Rehabilitation in a Mouse Model of Peripheral Nerve Injury

12.30 - 12.55 — **Younes Mokrab,** Sidra Medicine, Qatar

Title: Large-Scale Analysis of 6,000 Whole Genomes from Qatar Uncovers Genetic Structure of Arab and Middle Eastern Populations and Establishes A Valuable Resource for Understanding Personalized Disease Risk and Causality

12.55-13.20 **Omar Tluli,** Qatar University, Qatar

Title: microRNAs as Targets for Glioma Therapy

lunch 13.20-14.00

14.00 - 14.25 **N.M. Mamadshoeva,** I.M. Sechenov First Moscow State Medical University, Russia

Title: Strategies for the Prevention of Hereditary Diseases in A Republic of Tajikistan

14.25 - 14.50 **Luidmila Lazarenko,** Saint-Petersburg Pasteur Institute, Russia

Title: New Mutation in SERPING1 gene c. 860 T>G is a Associated with C 1-INH -HAE Type 1

14.50 - 15.15 **Ramadan Hassan,** El-Mansoura University, Egypt

Title: A Novel Pentavalent Vaccine Candidate Combining Outer Membrane Proteins with Capsular Polysaccharides Completely Protects Against *Acinetobacter baumannii*

15.15 - 16.40 **Xianjing Liu,** Erasmus MC University Medical Center, Netherlands

Title: Integration of AI-Based Phenotyping and Combined GWAS Reveal Novel Genetic Insights of Image-Based Complex Traits with Human Face as Example

16.40 - 17.05 Pier Giorgio Righetti, Politecnico di Milano, Italy

Title: Stalin Black dogs: A Post Mortem Diagnosis

17.05 - 17.30 Mohammed Merzah, University of Debrecen, Debrecen, Hungary

Title: Smoking-Associated Changes in Gene Expression in Coronary Artery Disease Patients Using Matched Samples

Day 1

Genetics 2023

Keynote Presentations

FERMENTATIVE GLYCOLYSIS CONTROLS TUMOR GROWTH, BACTERIAL, VIRAL INFECTIONS AND IMMUNITY: GENETIC DECONSTRUCTION AND THERAPEUTIC PERSPECTIVES

Pouysségur J[1,2], Marchiq I[1], Ždralević M[1] and Vucetic M[2]
[1]*University Côte d'Azur, (IRCAN), CNRS, France*
[2]*Centre Scientifique de Monaco (CSM), Monaco*

Abstract:

First I will present the most recent findings on fermentative glycolysis, a primitive / anoxic metabolic pathway at the root of life emergence on our planet. This pathway has retained the imprint of the origin of life without oxygen and has established itself, contrary to general belief, as the master and instrumental bioenergetic pathway for the rapid growth of cancers, tissues regeneration, immune cells, but also the rapid growth of pathogenic bacteria and viruses. Second, emphasis will be placed on the lactic acid, the end-product of the hypoxic-imprinted glycolytic pathway, able to move across the plasma membrane in both directions *via* monocarboxylate transporters (MCT1, MCT4) assisted with their chaperon CD147. Lactic acid contributes to cell-pH homeostasis impacting the complex tumor immune response *via* infiltration of the tumour micro environment. Third, we revisit 'Warburg effect' *via* CRISPR-Cas9 disruption of glucose-6-phosphate isomerase (GPI-KO) or lactate dehydrogenases (LDHA/B-DKO) in two aggressive tumours (melanoma, colon adenocarcinoma). Full suppression of lactic acid production reduces tumour growth 2 to 3-fold, while disruption of the lactic acid transporters MCT1/4 completely suppressed glycolysis, mTORC1 and tumour growth as a result of intracellular acidosis. Finally, we briefly discuss the current clinical developments of an MCT1 specific drug AZ3965, and expecting progress for a specific *in vivo* MCT4 inhibitor, two drugs of extreme high potential for future clinical applications against cancers, bacterial and viral pathogens.

Biography

Jacques Pouysségur, CNRS Research Director Emeritus, graduated from an Engineering School in Biochemistry of the University of Lyon, where he obtained his PhD in 1972. He spent two years as a post-doctoral scientist at the National Cancer Institute of NIH (USA) and established his own research group in 1978 at the CNRS Biochemistry Centre of the University of Nice. After directing the CNRS Institute of Signalling, Developmental Biology and Cancer Research up to 2008, his team joined the new Research Institute of Cancer & Aging (IRCAN) in Nice and the Biomedical Department of the Centre Scientifique of Monaco (CSM). *Jacques Pouysségur* has previous experience in bacterial and somatic cell genetics, metabolism, Na-H exchanger, pH regulation, G protein-coupled receptors and MAP kinase signalling in the context of growth control in mammalian cells. In the last 25 years his group developed a strong interest in hypoxia signalling, oxygen and nutrient sensing, angiogenesis, autophagy amino-acid transporters, oxidative stress, cancer metabolism, Warburg effect and immune-suppression. He is member of AACR, EACR, EMBO, the French and European Academy of Sciences and the past President of the International Advisory board of the National Cancer Institute.

HEREDITARY FUSION GENES AS THE DOMINANT "INHERITED" GENETIC FACTORS ASSOCIATED WITH HUMAN INHERITANCES

Degen Zhuo
Biotailor Inc, USA

Abstract:

It has been common knowledge that mutated genes are “inherited” genetic factors, and fusion genes are somatic and cancerous. However, during systematic validations of fusion genes discovered from RNA-Seq identified by SCIF (Splicing Codes Identify Fusion Transcripts), we have found that some fusion transcripts are present in healthy individuals at such high frequencies that it is mathematically impossible for fusion genes to be generated via somatic genomic abnormalities.

To simplify it, we have fusion genes into hereditary, epigenetic (readthrough), and somatic ones. The hereditary fusion genes (HFGs) are defined as the fusion genes offspring inherited from their parents, excluding the epigenetic fusion genes (EFGs) generated via cis-splicing of readthrough pre-mRNAs of two identical-strand neighboring genes. We systematically used monozygotic (MZ) twins as a genetic model to study HFGs and discovered 1180 HFGs. We have used these 1180 MZ HFGs to analyze fusion transcripts from multiple myeloma (MM), acute myeloid leukemia (AML), and amyotrophic lateral sclerosis (ASL). We have identified hundreds of HFGs associated with MM, leukemia, and ASL, ranging from 10% to 95%. We have identified the common “inherited” genetic factors associated with human diseases. For example, TPM4-KLF2 is detected in 92.2% of MM patients and 74.1% of AML, respectively. *ZNF528-ZNF880* and *ADAMTSL3-SH3GL3* have been detected in 98.7% and 87% of ASL patients, 94.1% and 82.4% of mesial temporal lobe epilepsy patients, 88.9% and 100% of Alzheimer’s disease patients, respectively. The numbers and frequencies of the HFGs are much larger than their counterparts of the mutated genes and support that HFGs are the dominant “inherited” factors and play a major role in human genetics and diseases. The HFG discoveries will change the paradigm of human genetics and complex diseases, leading to much earlier diagnosis and prevention of human diseases, from cancer to ASL.

Biography

Degen Zhuo is a Chief Scientist and President of SplicingCodes.com, BioTailor Inc. He had completed his PH. D, Molecular Biology (1989 - 1994) in University of Ottawa. He has been interested in theoretical models of pre-mRNA splicing specificity since he was going to graduate school. In 2006, he had discovered that recently-gained splicesomal introns have identical 5' and 3' splice sites. Based on this finding, they have found that 5' exonic (E5) and 3' intronic (E3) sequences are dynamically conserved and are similar to those of group-II ribozymes. They have proposed that 5' exonic (E5) and 3' intronic (E3) sequences constitute splicingcodes.

Day 1

Genetics 2023

Oral Presentations

GLUTAMATE TRANSPORTER MISSENSE MUTATIONS ASSOCIATED TO EPILEPTIC ENCEPHALOPATHY AFFECT BOTH, TRANSPORT AND CHANNEL FUNCTIONS.

Peter Kovermann and Christoph Fahlke
Forschungszentrum Jülich GmbH, Germany

Abstract:

Naturally occurring mutations in *SLC1A2* encoding the excitatory amino acid transporter 2 (EAAT2) have been associated with severe forms of early infantile epileptic encephalopathy. Affected children suffer from dramatic epileptic seizures with onsets at early postnatal ages and developmental slowing. EAAT2 is expressed in both, glial and neuronal cells and removes the neurotransmitter L-glutamate from the synaptic cleft. Beside its secondary active transporter function, EAAT-transporters also function as anion channels. How disease-associated mutations modify these two transport functions of EAAT2 and how such alterations cause epileptic syndromes is insufficiently understood. We studied the functional consequences of the three previously reported mutations in *SLC1A2* that cause amino acid exchanges p.Gly82Arg, p.Leu85Pro and p.Pro289Arg, by heterologous expression in mammalian cells, biochemistry, confocal imaging, and whole-cell patch clamp recordings of EAAT2 L-glutamate transport and anion currents. G82R and L85P exchange amino acid residues that contribute to the formation of the EAAT anion pore. They enlarge the pore diameter sufficiently to permit the passage of L- glutamate and thus function as glutamate efflux pathways and thus to impair efficient removal of L-glutamate from the synaptic cleft. The mutation P289R decreases L-glutamate uptake, but increases anion currents despite a lower membrane expression. A homologous mutation (P290R) has been identified in the human glial isoform EAAT 1 in a child with episodic ataxia 6, which results in epilepsy and ataxia. No homologous mutations in other EAAT isoforms have been reported for the pore mutations G82R and L85P, so far. L-glutamate permeability of the EAAT anion pore and impairments of L-glutamate uptake are important functional consequences of naturally of the tested missense mutations. Particularly, L-glutamate efflux through mutant EAAT2 anion channels will cause excitotoxicity and neuronal hyperexcitability in affected patients.

Biography

Peter Kovermann received his PhD in 2004 at the department of biophysics in the university of Osnabrück (Germany) for his dissertation in mitochondrial protein import. From 2004 to 2007, he worked as a postdoc at the University of Zurich (Switzerland) in the Institute for Plant Physiology on organellar ion channels in plants. In the following, he started his work in the group of Prof. Christoph Fahlke in the Institute for Neurophysiology at the Hanover Medical School and moved in 2012 with the group to the Forschungszentrum Julich. The main focus of Dr. Peter Kovermann is the functional characterization of neuronal and glial membrane proteins with an emphasis on disease-associated missense-mutations. His method spectrum encompasses biochemical and electrophysiological experiments on cell cultures or acute animal tissue slices and the behavioral testing of and immune histology of animal disease models. Another key aspect are fluorescence-based methods to study the ion concentrations and their homeostasis in cells or within organelles, and their pathological changes in neuronal disorders.

BENEFICIAL EFFECTS OF CHRYSIN ON CADMIUM-INDUCED NEPHROTOXICITY IN RATS: MODULATING THE LEVELS OF *Nrf-2*/HO-1, RAGE/NLRP3, AND Caspase-3/Bax/Bcl-2 SIGNALING PATHWAYS

Hasan Simsek
Aksaray University, Turkey

Abstract:

Cadmium (Cd) is a toxic heavy metal that targets the kidney directly in the body. Chrysin (CHR) is a natural flavonoid with many properties such as antioxidant, anti-inflammatory and anti-apoptotic. The current study discloses new evidence as regards of the curative effects of CHR on Cd-induced nephrotoxicity by regulating oxidative stress, apoptosis, autophagy, and inflammation. Cd was administered orally at a dose of 25 mg/kg body weight alone or in combination with orally administered CHR (25 and 50 mg/kg body weight) for 7 days. Biochemical, molecular, and histological methods were used to investigate inflammation, apoptosis, autophagy, and oxidant pathways in renal tissue. Renal function tests were also evaluated. Cd caused an increase in serum toxicity markers, lipid peroxidation and a decrease in the activities of antioxidant enzymes. Nrf-2 triggered inflammatory responses by suppressing HO-1 and NQO1 mRNA transcripts and increasing NF-κB, TNF-α, IL-1β and iNOS mRNA transcripts. Cd caused inflammasome by increasing RAGE and NLRP3 mRNA transcripts. In addition, Cd application caused apoptosis by increasing Bax, Apaf-1 and Caspase-3 mRNA transcripts and decreasing Bcl-2 mRNA transcript level. It caused autophagy by increasing the activity of Beclin-1 level. CHR treatment had the opposite effect on all these values and reduced the damage caused by all these signal pathways. Overall, the data of this study indicate that renal damage associated with Cd toxicity could be ameliorated by CHR administration.

Biography

Hasan Şimşek, who is currently working as a Research Assistant at Aksaray University Faculty of Medicine, Department of Physiology, received his Ph.D. degree from Afyon Kocatepe University Institute of Health Sciences, Department of Physiology (Medicine). His specialty is cellular and molecular physiology. He has worked on many projects in the field of physiology and has international articles and national and international papers from these projects. In the projects, he is generally a researcher using molecular analysis methods (DNA/RNA isolation, PCR, RT-PCR, agarose gel, UV imaging, Image J analysis) and the ELISA method. In addition, he has experience in determining the dose, administration, and follow-up of the necessary active substance in experimental animals and in surgical operations and removal of the necessary tissues. I have taken an active role in the preparation (determination of materials, directing purchases, preparation of necessary documents) and experimental stages of many scientific projects. He has participated in many national and international congresses and symposiums and presented oral or poster presentations at these events. He actively teaches Physiology courses in the Faculty of Medicine and Faculty of Veterinary Medicine.

DECIPHERING ETHNIC DISPARITIES IN BC GENOMICS: UNMASKING DRIVER GENES TO BRIDGE THE ONCOGENIC DIVIDE

Arwa Khashkhusha
University of Manchester, United Kingdom

Abstract:

Background: The international cancer genome consortium (ICGC) has made substantial progress in understanding the genomic landscape of many different tumour types, supported by the growing field of cancer genomics, leading to major discoveries in the areas of mutational signatures, driver discovery and tumour evolution, amongst others. Most of the human genetic diversity is found in the continent of Africa, yet only 2% of participants in Genome Wide Association Studies (GWAS) are of African ancestry, and ICGC included no projects based within Africa. In this project we aimed to analyse the DNA of breast cancers (BC) from Nigeria, Hong Kong and TCGA.

Aim: We aim to identify differences between patients of the varying ethnicities in genomic features, notably prevalence of mutations in driver genes. We hypothesise from our literature review that GATA3 and TP53 will be the most frequently mutated gene in our Nigerian cohort and Hong Kong population respectively. Finally, we expect to find no correlation evidence between BC driver genes in Hong Kong and Nigerian cohorts.

Method: To achieve this, we compiled a comprehensive driver gene list from a literature review of all the up-to-date publications. After which, we conducted a search on our samples to identify the presence of these drive genes using R code script. We then analysed the data to calculate frequency of driver gene co-occurrence. In addition, dNdScv is a program which we used to help distinguish between passenger and driver mutation and to calculate p value.

Results: We found the driver gene GATA3 and PIK3CA to be the most significantly mutated gene in the Hong Kong cohort. They were both also found to have a significant co-occurrence positive Log Odds ratio value with each other. The Nigerian cohort was noted to have TP53 as the most commonly mutated in dNdScv but we detected GRID1 to be of interest in our R script analysis.

Conclusion: By exploring genetic diversity in Hong Kong and Nigerian populations, a deeper understanding of breast cancer's molecular foundations can be achieved, aiding personalized treatment approaches. Distinct genetic profiles in these populations, identified using robust dNdScv analysis, highlight genes like GATA3 and GRID1 as promising subjects for further investigation. Future steps involve studying the mechanisms of these driver genes and potentially improving personalized diagnostics and treatment strategies.

Biography

Arwa khashkhusha is a medical student at the University of Liverpool. Besides studying, she spends much of my time researching into new medical advancements in genetics and AI, tutoring Alevel students and designing and developing websites. In 2019 she started tutoring part time for a few different organisations and found the satisfaction helping a student achieve their potential unmeasurable. She has then gone on to create a website with Alevel teaching and studying tips that she aspires to further grow.

CHALLENGES AND PRAGMATIC SOLUTIONS IN PRE-TEST AND POST-TEST GENETIC COUNSELING FOR PRENATAL EXOME SEQUENCING

Karin EM Diderich, Jasmijn E Klapwijk , Vyne van der Schoot, Hennie T Brüggenwirth, Marieke Joosten and Malgorzata I Srebniak
Erasmus MC, The Netherlands

Abstract:

The yield of genetic prenatal diagnosis has been notably improved by introducing whole genome chromosomal microarray (CMA) and prenatal exome sequencing (pES). However, together with increased numbers of diagnoses made, the need to manage challenging findings such as variants of unknown significance (VUS) and incidental findings (IF) also increased. We have summarized the current guidelines and recommendations and we have shown current solutions used in our tertiary center in the Netherlands. We discuss four of the most common clinical situations: fetus with normal pES results, fetus with a pathogenic finding explaining the fetal phenotype, fetus with a variant of uncertain clinical significance fitting the phenotype and fetus with a variant leading to an incidental diagnosis. Additionally, we reflect on solutions in order to facilitate genetic counseling in an NGS-era.

Regarding VUS, we discuss the role of our multidisciplinary team (MDT) in managing these in prenatal genetic diagnosis. In the past years, in 9/451 pregnancies tested with exome sequencing using a broad panel analysis a VUS was reported. We show the factors that were taken into account by the MDT, the crucial elements that enabled timely decisions on VUS disclosure and the follow up of these cases.

In addition, we will show the diagnostic yield (pathogenic and likely pathogenic variants that explained the fetal phenotype) of routine exome sequencing in fetuses with (multiple or isolated) ultrasound anomalies detected in the first two trimesters that had a normal molecular karyotype by chromosomal microarray. Our results indicate that a significant number of these fetuses with ultrasound anomalies carry a clinically relevant (likely) pathogenic variant that can be diagnosed through prenatal exome sequencing. In our opinion not only microarray testing, but also exome sequencing should be offered in cases of a fetus with ultrasound anomalies (regardless of the severity of the fetal anomalies).

Biography

Karin Diderich has been working as a clinical geneticist in prenatal genetics at the Erasmus MC in Rotterdam for the past 12 years. She is one of the leading members of the prenatal multidisciplinary team that works dedicated to patient care (counseling as well as diagnostics), education and clinical research related to the introduction of new techniques in prenatal diagnosis. The focus of the team is health care innovation and its proper implementation into routine counseling and diagnosis.

Karin is passionate about providing excellent prenatal care for pregnant women carrying a fetus with ultrasound anomalies. She was the key colleague who boosted the new workflow for rapid exome sequencing reducing the time between the invasive procedure and report of the genetic results while reducing ad hoc work.

In their research, the multidisciplinary team members focus on broad aspects of the introduction of new techniques in prenatal diagnosis including the selection of cases entitled to prenatal diagnosis, the diagnostic yield, incidental findings, uncertainty management, psychological aspects and the practical implementation.

Knowledge obtained by this research allows efficient introduction of health care innovation to the patient clinic as well as to (medical) students education.

APPLICATION OF NOVEL AI-BASED ALGORITHMS TO BIOBANK DATA: UNCOVERING OF NEW FEATURES AND LINEAR RELATIONSHIPS

K H Mok, Sherlock L, Martin B R and Behsangar S
Trinity College Dublin, Ireland

Abstract:

Our group has been developing analytical methods for metabolism and metabolites that involve a series of machine learning algorithms and artificial intelligence to identify multiple biomarkers from spectra obtained using high-resolution NMR spectroscopy. The method is designed to observe fluctuations in metabolite patterns and identify a coherent relationship among fluctuations and diagnose specific disease states or external perturbations such as diet or therapeutic intervention. Using this, we independently analyzed two large public domain datasets that contain ^{1}H-NMR spectral data from lung cancer and sex studies. Our approach of applying novel artificial intelligence (AI)-based algorithms to NMR is an attempt to globalize metabolomics and demonstrate its clinical applications. By enabling metabolite mapping in areas of localized enrichment as a measure of true activity, while also allowing for the accurate categorization of phenotypes, we have been able to uncover metabolites that had not been identified by the original studies involving these databases.

Biography

K.H. Mok is currently Associate Professor in Biochemistry (Trinity College Dublin), Director (ICMRBS), Editorial Board member (*Protein Journal* and *BioMed Res Intl*) and a member of the EUREKA IEP (Independent Evaluation Panel). Utilizing biomolecular NMR spectroscopy, his areas of interest are in NMR metabolomics and the structural biology of protein aggregation and intrinsically disordered proteins. Prof Mok's expertise in using NMR spectroscopy to elucidate structurally-fluid protein-fatty acid complexes has led to the development of 'Alpha1' by start-up company HAMLET Pharma, which has concluded successful Phase I/II studies as a bladder cancer therapeutic (Brisuda A et al, *Nature Commun* 2021).

DE NOVO MISSENSE MUTATIONS IN MPP2 CONFER INCREASED RISK OF VOGT-KOYANAGI-HARADA DISEASE BY TRIO-BASED WHOLE EXOME SEQUENCING

Xianyang Liu, Shengping Hou, Jiayu Meng, and Peizeng Yang
The First Affiliated Hospital of Chongqing Medical University, China

Abstract:

Vogt-Koyanagi-Harada (VKH) disease is one of the main causes of blindness among middle-aged and young people. However, the etiology of VKH disease remains poorly understood. Here, we conducted the first trio-based whole exome sequencing study in 25 VKH patients and 50 controls with follow-up study in 2,081 VKH patients from a Han Chinese population to uncover detrimental mutations. We identified 15 de novo mutations in VKH patients, one of the most important was Membrane Palmitoylated Protein 2 (MPP2) p.K315N. MPP2-N315 mutation showed strongly deleterious according to bioinformatics predictions. Additionally, this mutation was rare and was completely absent in 1000 Genome Project (1000g), The Genome Aggregation Database (GnomAD) and was very conservative in 10 species including Human, Rhesus Monkey, Mouse, etc. The subsequent functional studies showed that the inflammation phenotypes of clinical and pathological and retinal vascular leakage were aggravated in MPP2-N315 mutation knockin or MPP2-N315 adeno-associated virus treated mice with experimental autoimmune uveitis (EAU). In vitro, the secretory cytokines including IL-1β, IL-17 and VEGFA were increased in MPP2-N315 mutant ARPE19, in addition, the barrier function was destructed and the level of cell tight junction protein zonulaoccludens-1(ZO-1) was decreased. The mechanistic studies showed that MPP2-N315 mutation had stronger ability to directly bind to ANXA2 as compared with MPP2-K315 using LC-MS/MS and Co-IP, and then resulting in the activation of ERK3/IL-17 pathway. Collectively, our data demonstrated for the first time that MPP2-N315 mutation may increase the genetic susceptibility of VKH disease through ANXA2/ERK3/IL-17 pathway, and provided a new target for uveitis therapy.

Biography

Xianyang Liu was born in 1998 in China, a member of Chinese Genetic Society, currently working towards Ph.D. in Chongqing Medical University. He majored in ophthalmology under the supervision of Professor Shengping Hou. With more than four years of experience in genetic and immunological mechanisms of blinding eye diseases, he has mastered experimental technology skills and has been systematically trained to think scientifically. He has published several papers in good-impact journals as the author and co-author. At present, he identifies a de novo mutation MPP2-K315N in Vogt-Koyanagi-Harada (VKH) disease using whole exome sequencing (WES) study and explores the phenotypes and mechanisms of this mutation. This research has been under review status in the Cellular & Molecular Immunology journal. During his school years, he has a great passion for scientific research and sports, and has twice won the fifth place in Chongqing table tennis competition.

HYPERGLYCAEMIA INDUCES TGFβ1-DIFFERENTIAL GENE EXPRESSION IN PRIMARY HUMAN IMMUNE CELLS

Kareem Awad
Ruprecht-Karls University of Heidelberg, Germany

Abstract:

The diversity of metabolic reprogramming mechanisms in immune cells widely contributes to the genetic turn on in these cells. This genetic manipulation are of complex nature and rely on heterogeneous pathogenic/non-pathogenic stimuli (1-3). We aimed at studying the effect of hyperglycaemia on transforming growth factor beta 1 (TGFβ1) in immune cells and were able to demonstrate its dual role in monocytes/Macrophages as well as dendritic cells.

Furthermore, our results show how different pathogenic stimuli in normal and high glucose may modulate metabolism in immune cells and to what extent this could affect a different genetic cell map. Results show specific glycolysis/stimulus pattern suspecting a leading a role of TGFβ1 signalling under different glucose concentrations in human immune cells.

In conclusion, hyperglycaemia is an essential metabolic factor that based on the environmental stimuli of the immune cells may contribute to a different genetic status in these cells.

Biography

Kareem Awad research focuses on human immune cells responses to different pathogenic and non- pathogenic stimuli as well as the interaction of these cells with the surrounding nerves or vascular neighboring cells. So, his work within years of experiences in different scientific schools in Finland, Germany and Egypt investigated the responses of these cells to pathogens such as influenza viruses' strains as well as signals from abnormal environmental contexts such like hyperglycaemia or tumor cells. In this sense, he targeted diseases such as diabetes, influenza virus infection and cancer specifically the brain tumor glioblastoma. His last degree obtained from Cairo University is PhD in Pharmaceutical Sciences "Biochemistry".

UNDIFFERENTIATED ROUND CELL SARCOMA IN INFANT WITH BOTH CIC AND EWSR1 GENETIC ABERRATION: CASE REPORT

Milica Komnenić Radovanović[1], Marija Denčić Fekete[1], Ljubica Simić[1], Jelena Sopta[1], Milena Mihajlović[1], Savo Raičević[2] and Aleksandar Kostić[2]

[1]*University of Belgrade, Serbia*
[2]*University Clinical Centre of Serbia*

Abstract:

Introduction: The most common alterations in sarcomas are gene fusions and the large number of sarcomas are translocation related. Malignant mesenchymal tumours are very frequent and important in paediatric oncology, especially round cell sarcomas. In the latest WHO Classification of Bone and Soft Tissue 2022, beside the group representative and the most frequent round cell sarcoma in bone among pediatric population-Ewing sarcoma, there is a few relatively new entities named by the specific genetic aberration, formerly known as 'Ewing sarcoma-like tumors'. CIC-rearranged sarcoma (CRS) is one of them, and it is defined by its pathognomonic genetic signature and undifferentiated round cell phenotype. However, increasing data suggest that these tumors should be regarded as a stand-alone pathologic entity. In clinical practice, diagnosis of the oncogenic fusion is done using molecular techniques such as fluorescence in situ hybridization (FISH), reverse transcription polymerase chain reaction (RT-PCR), or targeted RNA sequencing.

Case presentation: We present a case of a two-year-old girl with expansive cerebral neoplasm in left temporal lobe, and severe headaches in the last period. Biopsy was performed. Tumor tissue showed diffuse and focally nodular growth, small to medium sized cells with hyperchromatic nuclei and countless mitoses. Morphological and immunohistochemical characteristics of the tumor excluded primary glial neoplasm, germ cell neoplasm, myogenic sarcomas, lymphoma and melanoma. Final pathohistological diagnose was high grade malignant mesenchymal neoplasm from the group of undifferentiated round cell sarcoma. Genetic analyses were needed to identify specific genetic aberration due to significantly differences in oncology treatment and prognosis between tumors of this group.

Method: We performed fluorescence in situ hybridization (FISH) on paraffin mold from the biopsy sample for *EWSR1, CIC* and *BCOR* gene rearrangement (BCOR Dual Color Break Apart Probe (Xp11.4), Dual color break-apart *CIC* Probe (19q13.2), Dual color break-apart *EWSR1* Probe (22q12)).

Results: By analyzing the above-mentioned mutations, we found a rearrangement in both the *CIC* and *EWSR1* gene. *BCOR* rearrangement was not detected. nuc ish(BCORx2)[100] nuc ish(EWSR1x2)[32/50], nuc ish(EWSR1x2)(5'EWSR1 con 3'EWSR1x1)(5'EWSR1 sep 3'EWSR1x1)[18/50] nuc ish(CICx2)[50/100], nuc ish(CICx2)(5'CIC sep 3'CICx1) [50/100]

Conclusion: According to results of the fluorescence in situ hybridization (FISH) this tumor was defined as a *CIC* rearranged sarcoma. *CIC* rearranged sarcoma is malignant neoplasm, most commonly found in deep soft tissue of young adults since now, even though it is described in wide age range. It is very uncommon and extremely rare in young pediatric patients, also in brain, with only few cases reported until now. Genetic analyses, beside *CIC* rearrangement in majority of tumor cells (50%), identified also *EWSR1* rearrangement in 36% of tumor cells. This result was unexpected, considering the etiology of the tumor itself and the literature data

known so far that these two genetic changes exclude each other. This genetic event could be explained as an associated genetic aberration of the single clone in a manner of tumor heterogeneity. Since, there is no data about tumor with both *CIC* and *EWSR1* genetic aberration, further studies are needed.

Biography

Milica Komnenić Radovanović master of molecular biology, specialist in medical genetics. For 13 years she was a geneticist in laboratory for Cytogenetics, Clinic for Ginecology and Obstretics, Clinical Centre of Serbia. For ten years she was in charge of running the laboratory and permanent Member of the Department for perinatal and reproductive endocrinology and genetics, Clinic for Ginecology and Obstretics, Clinical Centre of Serbia, working as a genetic counselor. Fot last two years she worked as geneticist in the laboratory for Molecular Pathology, Institute for Pathology, Medical University of Belgrade in the filed of molecular pathology (cytogenetic analysis, PCR and FISH analysis, Next Generation Sequencing Methods (NGS)). Co-author of several scientific papers published in various domestic and foreign journals and winner of a National fellowship ESHG Conference 2020 and National fellowship ESHG Conference 2022, elected by Serbian Genetics Society.

THORACIC AND ABDOMINAL AORTIC ANEURYSMS: EXPLORING THEIR CONTRAST AND GENETIC ASSOCIATIONS

Arwa Khashkhusha
University of Manchester, United Kingdom

Abstract:

Until recently thoracic aortic aneurysm (TAA) and abdominal aortic aneurysm (AAA) were correlated with atherosclerosis but following a range of cohort studies, a linkage proved unlikely. Instead, data from the Genome wide association study detected two common significantly correlated lncRNA loci: miRNA and the antisense non-coding RNA in the INK4 locus (ANRIL). lncRNAs are sometimes utilized by the body as transcription regulators and signaling molecules. This is crucial in cell transformation and embryology, including that of the mammalian heart. ANRIL, a 19 exon RNA sequence found in the chromosome 9p21 region, will be one of the main focuses of this paper. TAA and AAA have many differences due to their vessel walls but similarities in their gross anatomic structure prove a genetic correlated disease likely. ANRIL has a convincing potential to be used as an additive therapeutic tool in TAA and AAA. This is because Chr9p21 is independent of typical risk factors. However, it remains that further research and clinical studies are required before clinical translation. It is best to consider TAA and AAA separately as the underlying pathophysiology has some distinct differences. They are both commonly diagnosed late, and the hope is that genetic mutations (ANRIL) can act as a biomarker for a faster diagnosis, management and possible treatment alternative.

Biography

Arwa khashkhusha is a medical student at the University of Liverpool. Besides studying, she spends much of my time researching into new medical advancements in genetics and AI, tutoring Alevel students and designing and developing websites. In 2019 she started tutoring part time for a few different organisations and found the satisfaction helping a student achieve their potential unmeasurable. She has then gone on to create a website with Alevel teaching and studying tips that she aspires to further grow.

Day 2

Genetics 2023

Keynote Presentations

GENETIC DISSECTION OF ANTI-FERROPTOTIC AXIS REVEALS IRREPLACEABLE FACTORS FOR CANCER CELL SURVIVAL

Vucetic Milica[1], Daher Boutaina[1], Gotorbe Célia[1], Willian Meira[1], Durivault Jerome[1], Segui Fabien[1], Picco Vincent[1] and Pouyssegur Jacques[1,2]

[1]Centre Scientifique de Monaco (CSM), Monaco
[2]CNRS, INSERM, Centre A. Lacassagne, Faculté de Médecine (IRCAN), Université Côte d'Azur, France

Abstract:

Ferroptosis is newly described type of cell death, resulting in the oxidative damage of lipids in the plasma membrane, which leads to disturbed membrane integrity and selective permeability. Under physiological conditions ferroptosis is prevented by the antioxidant axis consisting of the enzyme glutathione peroxidase 4 (GPx4), its reducing power - glutathione (GSH), and the importer of oxidized cysteine (xCT), the rate limiting amino acid for synthesis of GSH. Large body of literature reported that interference with this axis, at any level, inevitably leads to cancer cell death by ferroptosis. Nonetheless, many of the studies based their conclusions on the findings obtained with pharmacological approach, i.e., with known inhibitors of the abovementioned anti-ferroptotic players, and mostly in in vitro conditions. Considering rising interests in ferroptotic inducers in the clinical settings, we aimed to investigate the redundancy of individual players as well as their potential as a target for anti-cancer therapy. Here I will present data we obtained using individual knockout of each of the anti-ferroptotic player and their effect on the tumor cell growth and survival, both *in vitro* and *in vivo*. Furthermore, I will give an overview of our data obtained with Warburg-null cells, which put ferroptosis sensitivity into general metabolic context of the cancer cell.

Biography

Milica Vucetic is a Post-Doctoral Researcher in Tumor Hypoxia and Metabolism Team at Centre Scientifique de Monaco, France. She developed Research themes such as Hypoxia signaling in cancers, Metabolic targets in cancer treatment, Role of hypoxia in metabolic reprogramming, HIF-1/AMPK interaction in phenotypic plasticity. She has published numerous research articles and papers in various high-ranking journals.

DECIPHERING NON-INVASIVE BIOMARKER POTENTIAL OF CIRCULATING MICRORNA IN PROSTATE CANCER

Mohammad Kaleem Ahmad and Anveshika Manoj
King George's Medical University, India

Abstract:

Background: Prostate Cancer (PCa) is a heterogeneous complex treated by invasive procedures like TURP, Radical Prostatectomy, or other ways leading to serious complications in one's life. In order to reduce these inconveniences, researchers are focused on circulating cell-free microRNA (miRNA) which are released into the blood serum/plasma as a result of apoptosis, necrosis, or secretions. Circulating miRNAs due to their resistance to degradation may act as potential biomarkers in early cancer detection, and provide therapeutic aid in better treatment of PCa.

Objective: Our study aims to explore and validate the expression of circulating miRNA in the serum of PCa patients and investigate their diagnostic potential in differentiating PCa from healthy controls.

Material and methods: The tissue and serum samples were collected from BPH and PCa patients and only serum samples from CRPC and healthy control for expression analysis of miRNA 183, miRNA 4510, miRNA 711, and miRNA 329. The diagnostic biomarker potential was evaluated using Receiver Operating Characteristics (ROC). Bioinformatic tools were used to explore and analyze miRNA target genes.

Results: Our study shows that miRNA 4510 and miRNA 183 were significantly upregulated and miRNA 711 and miRNA 329 were significantly downregulated in both PCa tissue and serum. ROC curve analysis shows good non-invasive biomarker potential of miRNA 4510 in both PCa and CRPC. The panel of miRNA constructed for PCa serum (miRNA 183-4510) and CRPC (miRNA 4510-329 & miRNA 183-711-329) had significant and greater AUC with higher sensitivity and specificity.

Conclusion: The estimation of cell-free miRNA and its target gene will give a wholesome picture of liquid biopsy for an individual- PCa patient and healthy control, which will help in reducing the pain and suffering of the patient as well as help in developing certain clinical tests that can help in quick and early diagnosis of PCa.

Biography

Mohammad Kaleem Ahmad's area of research is in molecular and cancer biology. He has attained an important experience in molecular as well as clinical cancer research. He was worked extensively in cancer therapeutics through the mechanistic evaluation of many natural agents against different cancer cell lines. Altogether he had published more than 100 research articles in reputed international journals with a total impact factor of over 200 and citations are more than 2000. Now he is working on microRNA profiling of prostate cancer and OSCC which may be useful as diagnostic and prognostic biomarkers for the prediction of therapy outcomes. Currently he is working as PI on the project entitled "Targeting non-invasive MicroRNAs as novel signature for castration resistance and aggressive prostate cancer: A case control study". The study focuses on a better understanding of miRNA-regulated pathways in prostate cancer can improve our knowledge in pathogenesis of the disease and can potentially aid in developing miRNA-based diagnostic and therapeutic strategies for the management of CRPC and prostate cancer

Day 2

Genetics 2023

Oral Presentations

GENOME SEQUENCING FROM 50 AUTISM TRIOS IDENTIFIED NOVEL CANDIDATE GENES WITH MIXED INHERITANCE PATTERN IN THE QATARI POPULATION

Vijay Gupta, Afif Ben-Mahmoud, Fouad Alshaban, Lawrence W. Stanton and Hyung-Goo Kim

Hamad Bin Khalifa University, Qatar Foundation, Qatar

Abstract:

The advent of next-generation sequencing (NGS) has revolutionized human genetics in rare genetic disorders, improving the diagnostic yield and reducing the turnaround time. Despite challenges related to deep reads and managing large dataset, genome sequencing has successfully identified genetic variants associated with ASD due to its extensive coverage. To address the underrepresentation of genetic studies on autism in the Middle East, we conducted genome sequencing on 50 trios of independent simplex autism families from Qatar with unknown etiology including 14 consanguineous and 36 non-consanguineous families, consisting of 41 males and 9 females. Our analysis revealed various types of variants, including de novo, homozygous, X-linked, and compound heterozygous variants, totalling 42-missense, 2-frameshift, 2-nonsense, 1-splicing, 1-in-frame 3 nucleotide deletion,1-start loss, and 1 >200 CGG repeats of FMR-1 variants. These variants were found in 30-known and 20-novel candidate genes, providing an aetiologic diagnosis. The pathogenicity of these variants was substantiated by CADD scores, their frequency in gnomAD, reported sporadic variants, and physical direct interaction with products of known ASD genes. Of the participants, comprising 41-males and 9-females, 40-individuals had syndromic ASD and 10-had non-syndromic ASD. The cohort comprised individuals from various backgrounds, including 33-Qatari (66%), 5-Syrian (10%), 2-Egyptian (4%), 2-Yemeni (4%), 2-Sudanese (4%), 1-Saudi Arabian (2%), 1-Algerian (2%), 1-Jordanian (2%), 1-Indian (2%), 1-Tunisian (2%), and 1-Palestinian (2%).The most common phenotypes observed among the probands included autism, intellectual disability, epilepsy, developmental disorders, and language/speech delay. Our preliminary findings illustrate the mixed inheritance patterns in autism families in Qatar, characterized by a high rate of consanguinity (52%). Additionally, our results highlight the association of ASD with fundamental cellular processes such as ion transport pathway, ubiquitin pathway, neuron migration, and transcription activity, which are crucial for normal cognitive development and function.

Biography

Vijay Gupta received his Ph.D. at the Centre for Cellular and Molecular Biology (CCMB), INDIA (2006). Dr. Gupta was granted multiple awards such as ASCB pre-doctoral travel award (2005), Carl Storm International Diversity Fellowship to attend the Gordon Research Conference (2006) and later on Royal Society International Incoming Fellowship (2006) from the Royal Society, London, UK to perform research at The University of Bristol. He joined The Scripps Research Institute, La Jolla, USA on Target Characterization Fellowship funded by Cystic Fibrosis Foundation, USA as CF fellow for five years and then moved to University of California, San Diego as Assistant Project Scientist where he worked till 2017.

Dr. Gupta has multidisciplinary research experience in the fields of protein trafficking, cancer and human genetic diseases and has published more than twenty publications including top-tier journals such as Nature Chemical biology, Developmental Cell, PNAS, JCS and Traffic. He is an invited member of Sigma Xi-Scientific Honor Society, Cell Stress Society International (CSSI), USA, peer review board member of JoVe and Dove press and has reviewed more than thirty manuscripts. One of the hobbies of Dr. Gupta is popular science writing for the general public, aimed at raising scientific awareness.

A COMPREHENSIVE REVIEW ON THE ROLES OF METALS MEDIATING INSECT–MICROBIAL PATHOGEN INTERACTIONS

Subhanullah Khan
University of Chinsese Academy of Sciences, China

Abstract:

Insects and microbial pathogens are ubiquitous and play significant roles in various biological processes, while microbial pathogens are microscopic organisms that can cause diseases in multiple hosts. Insects and microbial pathogens engage in diverse interactions, leveraging each other's presence. Metals are crucial in shaping these interactions between insects and microbial pathogens. However, metals such as Fe, Cu, Zn, Co, Mo, and Ni are integral to various physiological processes in insects, including immune function and resistance against pathogens. Insects have evolved multiple mechanisms to take up, transport, and regulate metal concentrations to fight against pathogenic microbes and act as a vector to transport microbial pathogens to plants and cause various plant diseases. Hence, it is paramount to inhibit insect–microbe interaction to control pathogen transfer from one plant to another or carry pathogens from other sources. This review aims to succinate the role of metals in the interactions between insects and microbial pathogens. It summarizes the significance of metals in the physiology, immune response, and competition for metals between insects, microbial pathogens, and plants. The scope of this review covers these imperative metals and their acquisition, storage, and regulation mechanisms in insect and microbial pathogens. The paper will discuss various scientific studies and sources, including molecular and biochemical studies and genetic and genomic analysis.

Biography

Subhanullah Khan is an accomplished researcher renowned for their expertise in neurodegenerative diseases, mainly focusing on the genetic foundations underlying these complex conditions. Holding a distinguished [Master's degree] in [Biochemistry and Molecular Biology], he was dedicated his career to advancing our understanding of the genetic intricacies driving neurodegeneration.

Day 2

Genetics 2023

Poster Presentations

CORRELATIONS BETWEEN GENOTYPE AND PHENOTYPE IN HEREDITARY HYPERFERRITINEMIA-CATARACT SYNDROME: AN ANALYSIS OF THREE BRAZILIAN FAMILY CASE SERIES

Zilton Vasconcelos, Olivia A Zin, Luiza M Neves, Daniela P Cunha, Fabiana L Motta, Bruna NS Agonigi, Dafne DG Horovitz, Daltro C Almeida, Jocieli Malacarne, Ana Paula S Rodrigues, Adriana B Carvalho, Cinthia A Rivello, Rita Espariz, Andrea A Zin and Juliana MF Sallum

National Institute of Women's Health Child and Adolescent Fernandes Figueira/Fiocruz, , Brazil

Abstract:

This case series highlights Hereditary Hyperferritinemia-Cataract Syndrome (HHCS), a rare autosomal dominant disorder often misdiagnosed due to its unique characteristics—pediatric cataracts and hyperferritinemia without iron overload—caused by mutations in the FTL gene. In this study focusing on three Brazilian families, the primary objectives are to raise awareness about HHCS and explore potential phenotypic relationships between FTL mutations and coexisting mutations in the HFE gene, responsible for autosomal recessive hereditary hemochromatosis. The investigation encompassed eight HHCS-afflicted individuals from the three families, and for trio analysis, one unaffected member from each family was included, totaling eleven participants. Rigorous ophthalmological and clinical genetic assessments were conducted. The prominent finding was the presence of the likely pathogenic c.-157G>A variant in the FTL gene across all affected family members. Their common manifestation involved gradual bilateral cataract development before the age of 14, characterized by diverse bilateral diffuse opacities. Hyperferritinemia was consistently observed among the affected individuals, with levels ranging from 971 ng/mL to 4899 ng/mL. Of particular interest, two affected individuals harbored a concurrent pathogenic variant in the HFE gene (c.187C>G, p.H63D), coinciding with the highest serum ferritin values in the cohort. While the co-occurrence of pathogenic mutations in both FTL and HFE genes is scarcely documented, this study accentuates the need for further research to elucidate potential phenotypic interactions contributing to elevated hyperferritinemia values. By shedding light on these intricate genetic associations and their resulting clinical implications, this case series aims to expand understanding of HHCS and its multifaceted phenotypic landscape.

Biography

Zilton Vasconcelos devoted his career to exploring rare diseases in pediatric medicine. As a researcher in public health at the National Institute of Women's Health Child and Adolescent Fernandes Figueira, his focus is on pediatric-related translational research. He started as a lab technician at the Brazilian National Cancer Institute during college, where he learned about immunological monitoring and CD34 quantification using flow cytometry. This experience fueled his interest in transplantation immunology, which he pursued during his MSc and PhD. After that, he joined his current institution, a hospital specializing in infant medical care, where he shifted his attention to primary immunodeficiencies. Additional training in this field came from Seattle Children's Hospital in the USA, where he learned about diagnosing these conditions. This was followed by a post-doc opportunity at INSERM in Toulouse, France, where he engaged in Wiskott-Aldrich Syndrome translational research. Back in Brazil, he now co-direct a laboratory within the same institute's clinical research unit. Their focus is on analyzing genetic and infectious diseases in rare pediatric cases. He was also involved in training young master's and PhD investigators dedicated to improving pediatric health, with a specific focus on rare diseases and congenital infections.

GENETIC VARIABILITY IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: INPUT FROM HIGH THROUGHPUT GENOME ANALYSIS

Chandra Devi[1], Sonam Raj[2], Shivendra Singh[1], Prashant Ranjan[1] and Parimal Das[1]

[1]Banaras Hindu University, India
[2]National Institutes of Health, USA

Abstract:

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a hereditary nephropathy affecting 1 in 500-1000 individuals globally. It is characterized by the gradual growth of multiple fluid-filled kidney cysts, often leading to end-stage renal disease. ADPKD exhibits genetic variability, with *PKD1 (85%)* and *PKD2 (8%)* mutations accounting for most cases, and ~7% of cases remaining genetically unexplained. The study employed whole exome sequencing (WES) to investigate disease-causing mutations in a trio with PKD, revealing a frameshift-deletion in the *MIOX* gene as a likely cause of the disease. Association of *MIOX* was not previously reported in ADPKD. *MIOX* encodes Myo-Inositol Oxygenase, which plays a role in renal myoinositol catabolism pathway. The study highlighted the potential of WES as a diagnostic tool for PKD and its implication for practicing personalized medicine.

Furthermore, the study analyzed gene expression profiles in cystic tissue samples from GEO dataset- GSE7869 and found a substantial reduction in *MIOX* gene expression compared to minimal cystic tissues and control samples suggesting the involvement of *MIOX* in the development of PKD and how the altered function of MIOX may lead to the formation of kidney cysts in ADPKD.

While WES of another proband of a separate family resulted identifying a likely pathogenic heterozygous nonsense variant, c.1777G>T (p.Glu593*), in the *PKD1* gene, associated with ADPKD manifestations, in another family, additional common variants were found in the *PKD1* gene in affected members along with variants in other genes (*C6orf226, LRPKD1B, PKD1P1, EME2, EMR2, KCNV2*). These findings shed light on the genetic complexity of ADPKD and emphasize the importance of genetic testing for accurate diagnosis and potential future therapeutic approaches. Overall, the study demonstrates the utility of WES in understanding the genetic basis of PKD and advancing precision medicine in this field.

Biography

Chandra has completed her under-graduation degree in Biotechnology (Hon's) from Himachal Pradesh University, Shimla, India and post graduation from Panjab University, Chandigarh, India. Her Postgraduate M.Sc. dissertation work with Prof. Tapas Mukhopadhyay focused on the effect of human-MDGI (Mammary Derived Growth Inhibitor) expression on the bacterial growth. Afterwards, she worked with Prof. Akshay Anand at Neuroscience Research Lab, Postgraduate Institute of Medical Education and Research, Chandigarh, India on Muscular Dystrophy (DMD, BMD). Currently she is pursuing PhD under the supervision of Prof. Parimal Das at Centre for Genetic Disorders, Banaras Hindu University, Varanasi, India and her work is mainly focused on genomics of Polycystic Kidney Disease. Their research is directing to shed light on the genetic complexity of PKD, understanding the involvement of the candidate and other genes and functional analysis of variations in disease development and progression especially in India. This will help paving the way for precision medicine approaches in PKD diagnosis and treatment.

A CASE REPRESENTATION OF AIP WITH PATHOGENIC MUTATION IN HMBS GENE

Abeer Zakariyah[1] and Sultan Altouri[2,3]

[1]University of Jeddah, Kingdom of Saudi Arabia
[2]King Fahad Armed Forces Hospital, Saudi Arabia
[3]University of Ottawa, Ottawa, ON, Canada

Abstract:

The hydroxymethylbilane synthase (HMBS) enzyme is involved in the production of heme. Mutations in the HMBS gene can lead to a deficiency of hydroxymethylbilane synthase. This can cause a buildup of porphyrins, which are precursors of heme. These porphyrins can damage the nervous system and other organs, leading to the symptoms of acute intermittent porphyria (AIP). AIP is an autosomal dominant disorder. There are over 400 different mutations in the HMBS gene that have been linked to AIP. In the current study, we are reporting a case of AIP. A 20-year-old female presented with acute abdominal pain, nausea, and vomiting. She had no prior medical history and was otherwise healthy. After a few weeks of investigation, the hematology team was consulted for suspicion of acute porphyria, and they sent an investigation for porphyria. Laboratory tests revealed elevated liver enzymes and a urine test for porphobilinogen. Genetic analysis showed that she had a splice variant mutation in the HMBS gene, which is associated with AIP. The following mutation was detected in a heterozygous state (c.826-2A>T) in the HMBS gene, which was previously reported to be pathogenic. She is currently being monitored by a hematologist. More genetic investigations are currently being conducted for the rest of her family. This case report highlights the importance of considering AIP in the differential diagnosis of patients with acute abdominal pain. Genetic testing is helpful in confirming the diagnosis and identifying other family members who may be at risk.

Biography

Abeer Zakariyah is an Assistant professor at Jeddah University, in the Department of Medical Genetics. She as two interested majors. The first one is investigating the causes for genetic disorders as well as modeling human disease using mouse models and stem cells.

PAVING THE WAY: PROGRESS IN TOOTH AGENESIS DIAGNOSTICS AND THERAPEUTIC SOLUTIONS

Prashant Ranjan and Parimal Das
Banaras Hindu University, India

Abstract:

Congenital Tooth Agenesis (CTA) refers to the failure of tooth eruption in the oral cavity due to disruptions in developmental pathways. Hypodontia, the absence of fewer than five teeth excluding the third molars, is more prevalent in certain populations. To date, five genes—MSX1, PAX9, AXIN2, EDA, and WNT10A—have been associated with CTA in humans.

Our study initially discovered the association between PAX9 and CTA (Nature Genetics-2000). We subsequently identified disease-causing mutations, including four novel pathogenic variants in PAX9 and EDA, in different families of Indian patients. These findings establish PAX9 as the strongest candidate gene for CTA. In the future, these variants can serve as efficient DNA-based diagnostic biomarkers. Additionally, we developed a bioinformatics methodology to identify therapeutic targets for mutant PAX9 variants. By analyzing previously identified PAX9 variants from the NCBI database and using various algorithm-based tools, we identified six highly pathogenic variants. Structural analysis revealed unique altered regions, including sites not directly involved in functional interactions but located near these regions. This led to the hypothesis that drugs targeting these therapeutic sites may restore the function of mutant PAX9.

Functional studies of the novel PAX9 variants revealed alterations in nuclear localization, DNA-protein interactions, and protein-protein interactions, both in vitro and in silico. Through molecular docking, we observed that Glycerol binds to therapeutic sites in PAX9. Further treatment of wild-type and mutant PAX9 with Glycerol in HEK cell lines resulted in the restoration of BMP4 expression, a gene crucial for tooth development, as detected by RT-PCR. Interestingly, BMP4 gene expression was downregulated in comparison to the wild-type.

Furthermore, missing teeth have been associated with ovarian and colorectal cancers, highlighting the potential for early prediction and the adoption of appropriate treatment strategies to improve long-term disease-free survival

These integrated approaches not only enable the detection of deleterious mutations in candidate genes like PAX9 but also pave the way for personalized/precision medicine in the field of CTA.

Biography

With a passion for Molecular Genetics of Mammalian Tooth Development and Agenesis, Prashant Ranjan has emerged as a dedicated researcher in the field of dentistry. This interest took root during their work on "In silico DNA Protein interaction study on Wild and Mutant sequences of PAX9" alongside Prof. Parimal Das during and after completing a One-year post-graduate diploma in Chromosomal Genetics & Molecular Diagnostics (PGDCMD) at the prestigious Centre for Genetic Disorders, BHU, Varanasi, India.

Having already earned an MSc in Bioinformatics from BIT Mesra, Ranchi, India, Prashant Ranjan is driven to unravel the intricacies of congenital tooth agenesis in humans, seeking to understand the underlying causes of tooth developmental failure during organogenesis. Their research combines experimental, bioinformatics, and theoretical methodologies to evaluate the pathogenic potential and determine probable etiologies for tooth agenesis. Prashant delves into the realm of drug-targeted therapy for tooth regeneration, exploring innovative ways to promote dental health and restore tooth development.

Day 2

Genetics 2023

Video Presentations

INFLAMMATORY DETERMINANTS AND ASSOCIATED MORBIDITY IN HEMODIALYSIS PATIENTS

Roxana Villanueva Macedo, Claudia Jackelin De la Cruz-Ahumada , Jorge Fernando Topete-Reyes,Juan Pablo Mena-Ramírez, Juan Manuel Guzmán-Flores, Jesúa Ivan Guzmán-González, Saúl Ramírez-De los Santos and Denisse Arellano Mendez.

Los Altos University Center, Mexico

Abstract:

Worldwide, chronic kidney disease (CKD) affects eight to sixteen percent of the population. It is a leading cause of morbidity and mortality, and this implies a high social burden. CKD greatly impairs individuals' quality life, especially in those with the most advanced stages or who are on replacement therapy. Hemodialysis continues to be the most common form of replacement therapy ; despite its advantages, hemodialysis entails a reduced adherence to treatment, poor eating habits, and low physical activity, which in turn further impair the patient's physical, functional, metabolic, social, and mental status. In addition, adverse therapeutic effects may complicate the clinical picture.

Hemodialysis deteriorates patients' physical, metabolic, and mental status. Clinical outcomes derived from inflammation determine a worse status but are less frequently identified. The objective of the study was to identify inflammatory determinants and the effect of SNP-related serum IL-6 and IL-10 levels on associated morbidity in hemodialysis. A sample of hemodialysis patients at IMSS Regional Hospital No.46 in Guadalajara (n = 85) were tested using the Malnutrition Inflammation Score (MIS) and Patient Health Questionnaire-9 (PHQ-9) to assess the associated morbidity. Serum cytokine levels were quantified by enzyme-linked immunosorbent assay (ELISA). The restriction fragment length polymorphism (RFLP) technique was used for analysis of IL-6-572C/G and IL-10-1082A/G. Using data visualization methods, we identified relevant determinants of inflammation. A simple regression model was constructed between predictors and targets with genotypes as covariates. Results showed malnutrition in 85.9% of patients and depressive symptoms in 50.6%. IL-10 was the most relevant inflammatory determinant, with regression coefficients (R2) between 0.05 and 0.11. The GG genotype of IL-10-1082 A/G evinced small effect on both clinical outcomes (δ of 0.35 and 0.37, respectively). Hemodialysis increases the associated morbidity, cytokines act as inflammatory determinants, and genetic variability contributes to the severity of clinical outcomes. Further studies need to refine the causal relationship between inflammation and CKD.

Biography

Roxana Villanueva Macedo have graduated as a physician and currently a third year resident of Nephrology at the 46th Regional General Hospital of the Mexican Institute of Social Security in Guadalajara, Jalisco, Mexico. In addition to her hospital practice, she dedicated her research with the group formed by Dr. Topete, Ramirez de los Santos and other important collaborators. Thesir group in Mexico has special interest in conditions such as: Chronic Kidney Disease, Glomerulonephritis, Diabetic Kidney Disease and Bone Mineral Disease. In the case of this work they had one objective: patients who were in renal support therapy type haemodialysis and the measurement of proinflammatory cytokines related to polymorphisms. With quite interesting and relevant results for clinical practice.

NEW MUTATION IN SERPING1 GENE C. 860 T>G IS A ASSOCIATED WITH C 1-INH -HAE TYPE 1

Lazarenko L[1,2],Sedykh A[1], Ostankova J[1], Savin T[1,2] and Totolian Ar[1,2]

[1]*Saint-Petersburg Pasteur Institute, Russia*
[2]*First Pavlov State Medical University of St. Petersburg, Russia*

Abstract:

Introduction: HAE is a rare disease with an autosomal dominant type of inheritance that affects approximately one in 50,000 people worldwide. HAE exhibits swelling in various parts of the body, which differs from histaminergic edema of 1-4 days in duration. These edema are dense to the touch, cause patients a feeling of soreness and bursting surrounding tissues. Edema are resistant to antihistamine therapy and are threatening when localized in the larynx, accompanied by abdominal attacks and often by specific dermatological phenomena called "marginal erythema". Such angioedema are unpredictable, appear after mechanical trauma and are associated with estrogen (menarche, pregnancy, contraception). HAE disrupts the quality of life of patients, accompanied by the development of depression and other disorders in the psycho-emotional sphere.

Materials: We investigated a family in Kronstadt, the town near Saint-Petersburg where the four generations suffered from angioedema, which lasted for several days, refractory to antihistamine drugs, accompanied with vomiting, abdominal attacks, marginal erythema. The true diagnosis has been unloaded for several decades. Routine analyses confirm the diagnosis of hereditary angioedema: low C4 complement fraction and C1 inhibitor (quantitative and functional). It was surprising, that we discovered unknown earlier mutation in gene SERPING1.

Methods: The patient's whole blood was the material. From the sample DNA was extracted using the test system «Ampley-Prime Ribo-Prep» (FBUN CNIUM). Nucleotide sequences of the exon SERPING1 gene were determined by directly sequencing Sanger fragments using ABIPRISM 3500(AppliedBiosystems,USA).

Results: Direct sequencing to confirm the diagnosis by Sanger of eight exons of the SERPING1 gene whose mutations are associated with development of hereditary angioedema. As a result of research in 5 gene exon SERPING1 was first identified as mutating c. 860 T>G in the heterozygous state. The mutation found results in the replacement of the amino acid leucine with arginine at 287 position in the SERPING1 protein.

Conclusion: Thus, the typical clinical picture of edema, hereditary aggravation, presence of laboratory parameters, indicating a decrease of C4 complement fraction, a decrease of C1 inhibitor (qualitatively and functionally) allow to diagnose hereditary angioedema. In this way we believe that we have a case with a new mutation in gene SERPING1 associated with hereditary angioedema.

Biography

Lazarenko Luidmila M.D, Ph.D, an expert in allergy and clinical immunology. She is a member of EAACI, BSACI, RAACI, an author of one patent and more than 50 articles, devoted in allergy and clinical immunology.

Virtual Presentations

Virtual

Genetics 2023

Oral Presentations

A NOVEL MECHANISM PROMOTES ACTIN PATCH FORMATION TO PREVENT CHROMATIN BRIDGE BREAKAGE IN CYTOKINESIS

Eleni Petsalaki, Sofia Balafouti and George Zachos
University of Crete, Heraklion, Greece

Abstract:

Chromatin bridges are strands of incompletely segregated DNA connecting the anaphase poles or daughter nuclei. If unresolved, chromatin bridges can break in cytokinesis leading to micronuclei formation and accumulation of DNA damage. To prevent this, human cells form accumulations of polymerized actin (actin patches) at the base of the intercellular canal to stabilize chromatin bridges; however, the molecular mechanisms involved are incompletely understood. In the present study, we identify small GTPases, which control the growth or contraction of filamentous actin fibers, that localize to actin patches and are required for stable chromatin bridges in cytokinesis. Inhibition of these actin regulators reduces actin patch formation and promotes chromatin bridge breakage by confocal microscopy analysis of fixed cells or live-cell fluorescence microscopy. Furthermore, chromatin breakage in cells deficient for the above proteins is not caused by premature abscission, but correlates with reduced actin patches compared with wild-type cells. We also propose that DNA bridges generate tension inside the nucleus which is then transmitted through specific mechanosensitive complexes to the cell cytoskeleton to promote generation of actin patches in the cytoplasm. This study identifies a novel signaling pathway that prevents chromatin bridge breakage by promoting actin patch formation in cytokinesis in human cells. Because chromatin breakage can lead to genomic instability that is associated with cancer formation or progression, understanding how cells stabilize chromatin bridges may help us understand mechanisms of tumorigenesis.

Biography

Eleni Petsalaki completed her PhD in Molecular Biology and Biomedicine at the Department of Biology of the University of Crete in Greece in 2014, and has continued working as a post-doc in Dr George Zachos' lab of Cell Cycle and Division since. Her main research interest is to understand fundamental mechanisms of mitotic cell division in human cells and how mis-regulation of these mechanisms can lead to tumour formation and progression, with the aim to identify potential targets for cancer therapy. Her work has described several novel molecules and biochemical pathways that participate in the mitotic spindle and abscission checkpoints, two cell surveillance mechanisms that protect against erroneous chromosome segregation or chromatin damage during cell division. She has published 14 papers in leading scientific journals (13 first author publications) such as the Journal of Cell Biology (5), Nature Communications (1), Journal of Cell Science (2) and others, and her work has received >300 citations so far. She is a member of the Biochemical Society (FEBS), the American Association for Cancer Research (AACR), and the Royal Society of Biology (RSB), and an Ambassador of the American Society for Cell Biology (ASCB).

ALZHEIMER DISEASE: IS DISEASE RELATED TO GENES

Niharika Lal
Metro College of Health Sciences and Research, India

Abstract:

The brain is astounding organ, responsible for all the body functions. It weighs, at just 2% of total body weight, and is most complex structure. The three pound organ programs and controls particulars from surrounding world, and personifies the essence of mind and soul. Intelligence, creativity, emotion, and memory are a few of the many things governed by the brain. But, what happen if the brain slowly shrinks and dies. The coordination's of body monitored by nerve cell will be working slowly and the brain signals that are essential for life will not work properly. The condition is an indicative of Alzheimer disease (AD) or dementia, which initiates with mild memory loss, affecting over 30 million people worldwide.

People suffering from AD gently loss senses, thinking, reasoning ability, or comprehension. There will be a personality and behaviour changes which would be responsible for significant mood shifts and person may become anxious, agitated and delusional. The event of this illness likewise hugely affects life of patient's family, in addition to high financial expense to society. As the disease progresses, the person would need aid in all phases of life including, bathing, eating, motions, and using the rest room. The disease not only affects the individual but also the family, friends as seeing loved ones change from the known to a unknown ones impacts their psycho social behaviour.

There's no solution for Alzheimer's, yet one treatment may possibly defer decline from the disease, and there are drug and non-drug choices that may help treat symptoms. Understanding accessible options can help people living with the disease and their caregivers to cope with symptoms and improve the quality of life.

Most of scientist have accepting that AD is a genetic disease by locating genes that may cause some kind of early onset AD. The researchers are still working to reveal possible connections between the environment and genetics in many types of dementia. The present oral presentation will discuss about possible causes of AD and its association with genes.

SYNTHESIS, BIOLOGICAL AND MOLECULAR DOCKING STUDIES OF PYRIMIDINE-DERIVED BIOACTIVE SCHIFF BASES

Muhammad Adnan Younis and Saira Manzoor
Shenzhen University, China

Abstract:

Pyrimidine which is an important constituent of the genetic material of deoxyribonucleic acid, is identified with a large number of biological activities. Based on this, pyrimidine-derived Schiff bases (1-6) of hydroxy-1-naphthaldehyde were synthesized by using the condensation method. In addition, the molecular docking studies against topoisomerase II DNA gyrase, human hematopoietic cell kinase, urate oxidase from Aspergillus flavus, and cyclin-dependent kinase 8 to explore the antibacterial, antioxidant, antifungal, and anticancer properties respectively and binding affinities through bioinformatics approaches to determine the interaction among active molecules with the receptor. Hence, the computational docking analyses identified that all synthesized pyrimidine Schiff bases (1-6) are active and exhibited better binding affinities as compared to the standard drugs. Furthermore, all the prepared materials were characterized by using nuclear magnetic resonance, infrared, and elemental analysis. Additionally, the phasetransition and thermal decomposition temperatures were determined by differential scanning calorimetry and thermo-gravimetric analysis measurements. Moreover, the structures of pyrimidine-derived Schiff bases 1, 2, 3, 4, and 5 were also confirmed by the X-ray single-crystal diffraction technique. The pyrimidine-derived Schiff bases 5 possess significant antibacterial, antioxidant, antifungal, and anticancer agent properties which confirms its promising biologicalactivities over standard drugs.

Biography

Muhammad adnan younis obtained his Ph.D. degree in 2020 from Zhejiang University, Hangzhou, China. Currently, he is working as a postdoctoral fellow in Shenzhen University under the guidance of Prof. Tian Bingbing. His primary research interest is the synthesis, characterization, properties, and application of carbon-based materials for environmental and energy applications.

ASSESMENT OF GUT BACTERIAL PROFILE IN DIABETIC PATIENTS UNDERGOING BARIATRIC SURGERIES USING QUANTITATIVE PCR

Sara Minaeian, Mahnaz Dabagh, Soheil Rahmanifard, Milad Sabaie, Amir Hozhabrpour, Fateme Faraji and Abdolreza Pazouki

Iran university of medical sciences, Iran

Abstract:

Background & aim: In recent years, studies regarding the association of gut microbiome and multifactorial genetic disorders such as diabetes, has gained a lot of traction. Furthermore, metabolites excreted from gut microbiota have broad effects on genes responsible for a wide range of human disorders. The aim of this study was to evaluate changes in gut bacterial load in obese diabetic patients undergoing bariatric surgery.

Methods: Thirty obese and eligible patients were recruited from the Obesity Clinic of Rasool-E-Akram Hospital Complex in Tehran, Iran between May 2021 to May 2022. Blood and stool samples were collected from patients at two time-points: (1) before surgery (2) 6-months after surgery. These samples were used to determine the effect of the surgery on metabolic indices and gut microbiota via quantitative PCR.

Results: Bariatric surgery showed tremendous potential for alleviating the metabolic imbalance. Analyzing patient subgroups revealed that these surgeries can effectively alter the level and ratio of gut bacteria in diabetic patients with habit of volume eating. In these patients the relative proportion of *Bifidobacter* to *Lactobacillus* and *Bifidobacterium* to total load were decreased, while proportions of *Bacteriodetes* to *Bifidobacterium* and *Provetella* to *Bifidobacterium* were significantly increased.

Conclusion: Gathered results regarding changes in gut microbiota profile of diabetic patients and alleviation of the existing dysbiosis can be used as a potential therapeutic approach in treatment.

Biography

Sara Minaeian is the head of the Antimicrobial Resistance Research Centre, Institute of Immunology and Infectious Diseases, Rasoul-e-Akram Hospital, Iran University of Medical Sciences, Tehran, Iran. She is a microbiologist with interests in antimicrobial resistance and microbiota. The aim of her research is to help reduce microbial resistance and treat various diseases by studying the microbiome. She has gained her valuable knowledge through years of experience in research, evaluation, teaching and administration both in hospital and education institutions.

EVALUATION OF ANTIBACTERIAL POTENTIAL OF *PENICILLIUM* SPECIES AND GC-MS METABOLIC PROFILING OF *PENICILLIUM NIGRICANS*

Hafiza Farhat and Shahid Ullah
Gomal University D.I Khan, Pakistan

Abstract:

Endophytes have been identified as a viable source of therapeutically useful chemical compound with relevance in nowadays medicine, agriculture and pharmaceutical industries. Hence, there is a recent prospect of developing new drugs that are effective candidates to treat emerging diseases among plants, humans and animals. Initially different plants samples were collected from different areas for the isolation of endophytic *Penicillium* species. PDA media were used for the pure culture formation. The *Penicillium* species were further used for *in vitro* activity. Their antimicrobial potential were checked against five common laboratory bacteria (*Salmonella typhimurium, Pseudomonas aeruginosa,* and *E.coli, Bacillus subtilis* and *Staphylococcus aureus*). The *Penicillium* nigricans species were used for further study for the characterization of compounds by GC-MS technique. The *Penicillium* species were shown a major zone of inhibition against the five common laboratory bacteria. *Penicillium nigricans* showed the major zone of inhibition, and were further selected for GC-MS metabolic profiling. Several compounds were isolated from *P. nigricans* and were considered for having potential against bacteria. The compounds which were isolated for the first time as confirmed by computer matching against National Institute of Standards and Technology, USA (NIST Mass Spectrometry Data Center (mainlib) and finally compared with Science finder. The isolated compounds are; (R)-(-)-14-Methyl-8-hexadecyn-1-ol, Columbin, -7Octadecenoic acid, methyl ester, 9,12-Octadecadienoic acid, ethyl ester and Octadecanoic acid, ethyl ester. Endophytic fungi are now considered an excellent source of various effective bioactive natural products. The vital utilization of these fungi can provide benefit to the current demand for novel molecules for pharmaceutical, medical and agriculture industries. Large scale production of these bioactive metabolites is a major challenge to the world of science.

Biography

Hafiza Farhat did Ph.D on Antibiotic producing endophytic fungi associated with healthy plants and received Ph.D degree from university of Karachi. Now she is serving in well renowned and Public Sector University (Gomal University D.I Khan) of Pakistan as an Assistant Professor. She has research articles in high impact factor journal in national and international journals. She attended so many conferences and workshop as a speaker. She is a also gold medalist as she achieved two gold medals in University level by getting first position in M.Sc

CHITOSAN-COATED NANOPARTICLES OF *CALOTROPIS PROCERA* ESCALATE FUNCTIONS REHABILITATION IN A MOUSE MODEL OF PERIPHERAL NERVE INJURY

Tehreem Iman, Rabia Akram, Faiqa Sajid and Ghulam Hussain
Government College University Faisalabad, Pakistan

Abstract:

People deal with dominant and challenging health problems caused by peripheral nerve injuries (PNIs). These are some of the most typical forms of injuries. From traumatic causes, most peripheral nerve injuries occur and they affect the upper limbs. The scientific community, plastic surgeons, and neurologists to neuroscientists are the experts in the field of PNI. Full functional recovery is still infrequent, despite attempts. Numerous medicinal plants have shown some confirmation of effectiveness and diverse effects in many neurological and other diseases. In a mice model for maintaining peripheral nerve injury, the role of chitosan-coated nanoparticles of *Calotropis Procera* (*Calotropis procera*/Cht-NPs) was determined. It is the goal of this study. In living animals, to investigate the process of peripheral nerve injury experimental models have been created. Mice were divided evenly into two groups after the phase of acclimatization. In the treatment group (group 2) gavage with *C. procera*/Cht-NPs (2.5 mg/kg/day) on the other hand, normal chow was given to the control group. The right sciatic nerve of animals was mechanically crushed. For the evaluation of sensorimotor function recovery, behavioral analyses (hot plate, grip strength, SFI, and pinprick test) were performed. For the evaluation of oxidative stress, blood was drawn. With a statistically significant difference ($p<.05$), *C. procera*/Cht-NPs support the motor and sensory function retrieval after the PNI. Our research reveals it. In conclusion, a function restoration enhancing effect is shown by the *C. procera*/Cht-NPs. More thorough research for their use as a therapeutic agent is highly suggested.

Biography

Eleni Petsalaki completed her PhD in Molecular Biology and Biomedicine at the Department of Biology of the University of Crete in Greece in 2014, and has continued working as a post-doc in Dr George Zachos' lab of Cell Cycle and Division since. Her main research interest is to understand fundamental mechanisms of mitotic cell division in human cells and how mis-regulation of these mechanisms can lead to tumour formation and progression, with the aim to identify potential targets for cancer therapy. Her work has described several novel molecules and biochemical pathways that participate in the mitotic spindle and abscission checkpoints, two cell surveillance mechanisms that protect against erroneous chromosome segregation or chromatin damage during cell division. She has published 14 papers in leading scientific journals (13 first author publications) such as the Journal of Cell Biology (5), Nature Communications (1), Journal of Cell Science (2) and others, and her work has received >300 citations so far. She is a member of the Biochemical Society (FEBS), the American Association for Cancer Research (AACR), and the Royal Society of Biology (RSB), and an Ambassador of the American Society for Cell Biology (ASCB).

LARGE-SCALE ANALYSIS OF 6,000 WHOLE GENOMES FROM QATAR UNCOVERS GENETIC STRUCTURE OF ARAB AND MIDDLE EASTERN POPULATIONS AND ESTABLISHES A VALUABLE RESOURCE FOR UNDERSTANDING PERSONALIZED DISEASE RISK AND CAUSALITY

Younes Mokrab[1,4,6], Rozaimi Mohamad Razali[1,6], Juan Rodriguez-Flores[2], Mohammadmersad Ghorbani[1], Haroon Naeem[1], Waleed Aamer[1], Elbay Aliyev[1], Najeeb Syed[1], Fazulur Rehaman Vempalli[1], Hakeem Almabrazi[1], Ramzi Temanni[1], Li Liu[1], Guishuang Wang[1], Muna Al Hashmi[1], Wei Liu[1], Ahmed El Khouly[1], Shafeeq Poolat[1], Tariq Abu Zaid[1], Sara Tomei[1], Stephan Lorenz[1], Rashid Al-Ali[1], Andrew G. Clark[3] and Khalid Fakhro[1,4,5]

[1]Human Genetics Department, Sidra Medicine, Qatar
[2]Department of Genetic Medicine, Weill Cornell Medicine, USA
[3]Department of Molecular Biology and Genetics, Cornell University, USA
[4]Weill Cornell Medicine-Qatar, Qatar
[5]College of Health and Life Sciences, Hamad Bin Khalifa University, Qatar
[6]Department of Biomedical Science, College of Health Sciences, Qatar University, Qatar

Abstract:

Middle Eastern populations are largely understudied, notably their genetic structure, history as well as underlying disease risk and architecture. We present an in-depth analysis on a novel set of 6,218 whole genomes sequenced at 30x coverage from the Qatar Genome Program (QGP). This revealed extensive diversity as well as genetic ancestries representing the main founding Arab genealogical lineages of Qahtanite (Peninsular Arabs) and Adnanite (General Arabs and West Eurasian Arabs). Peninsular Arabs were found to be the closest relatives of ancient hunter-gatherers and Neolithic farmers from the Levant, and founder Arab populations experienced multiple splitting events 12–20 kya, consistent with the aridification of Arabia and farming in the Levant, giving rise to settler and nomadic communities. As far as recent genetic flow is concerned, these ancestries were found to contribute significantly to European, South Asian as well as South American populations, likely as a result of Islamic expansion over the past 1400 years. In terms of runs of homozygosity (ROH) which are known to be a risk for recessive disease, we found unprecedented lengths ROH particularly amongst Peninsular Arabs, extending to 60-70 Mb. Furthermore, we characterize a cohort of 1,491 men with the ChrY J1a2b haplogroup, identifying 29 unique sub-haplogroups (based on 103 novel SNVs), representing the largest set of subjects sequenced to date with this haplogroup. Based on this QGP dataset of predominantly healthy adults, we built an imputation panel containing 12,432 haplotypes and 69,018,172 SNVs. This provides unprecedented panel to expand genomic knowledge of Middle Eastern populations, empowering precision genomics studies in the region and worldwide.

Biography

Younes Mokrab is an established geneticist, bioinformatician and a leader in medical and population genomics with > 20 years' experience from world-renowned institutions in academia, big pharma, and healthcare. Currently he is acting director of Population Genomic Medicine Department, principal investigator and lead of the Neurological Disorders Research Program at Sidra Medicine and Adjunct faculty at Weil Cornell Medicine and

Qatar University. Prof. Mokrab Holds a PhD in Bioinformatics from the University of Cambridge UK and a postdoc from the University of Oxford investigating the molecular basis of channelopathies. Subsequently worked in in silico biopharmaceutical engineering at Lonza biologics, before joining Eli Lilly where he used computational genomics methods to explore the genetics of Schizophrenia and other neuropsychiatric disorders to identify and validate novel drug targets, collaborating with the PGC consortium. Prof. Mokrab joined Sidra Medicine in 2015, establishing a research lab leveraging genomics and biodata to study population structure and rare diseases in Middle Eastern populations, notably neurodevelopmental disorders with a translational focus on precision diagnosis and tailored therapy. Also, his lab has led efforts in building genomic and transcriptomic references for the Middle East as tools for precision medicine. Prof. Mokrab is a recipient of multiple research grants (>$5 m) and author of >60 articles in journals including Nature, Cell and Lancet. He is also a reviewer for high impact journals including Nature, and Nature Genetics. Prof. Mokrab has chaired in the organization of multiple conferences in the UK and Qatar and serving at various committees and advisory boards. He is a co-founder of the Qatar Genome Program Research Consortium, and an active member of international consortia including PGC, TGGA and HPRC.

microRNAS AS TARGETS FOR GLIOMA THERAPY

Omar Tluli
Qatar University, Qatar

Abstract:

Gliomas, which arise from glial cells in the brain, remain a significant challenge due to their location and resistance to traditional treatments. Despite research efforts and advancements in healthcare, the incidence of gliomas has risen dramatically over the past two decades. The dysregulation of microRNAs (miRNAs) has prompted the creation of therapeutic agents that specifically target them. However, they are involved in complex signaling pathways that contribute to the loss of expression of tumor suppressor genes and the upregulation of the expression of oncogenes. In addition, numerous miRNAs promote the development, progression, and recurrence of gliomas by targeting crucial proteins and enzymes involved in metabolic pathways such as glycolysis and oxidative phosphorylation. However, the complex interplay among these pathways along with other obstacles hinders the ability to apply miRNA targeting in clinical practice. This highlights the importance of identifying specific miRNAs to be targeted for therapy and having a complete understanding of the diverse pathways they are involved in. Therefore, it is of utmost importance to have a complete understanding of the role of miRNAs in the progression and prognosis of gliomas, the different pathways involved, and with special emphasis on identifying potential therapeutic targets.

Biography

Omar Tluli is a 20-year-old currently in his third year of medical school at Qatar University. Omar's journey is characterized by his unwavering passion for research, particularly in the realm of developing therapeutic agents, which has set him on an extraordinary path in the field of medicine. Omar's gift for communication and presentation skills led him to become a peer tutor at Qatar University for multiple medical subjects. He aspires to share his knowledge, whether through dynamic conference presentations or by contributing to the growth of healthcare in hospital and educational settings. Furthermore, Omar's publication in collaboration with Sidra Medicine about Gliomas holds promise in the world of research. Currently, he is deeply immersed in multiple laboratory projects, each brimming with valuable data awaiting publications. These publications stand as beacons of hope for discovering new therapies and enhancing healthcare practices, underscoring Omar's pivotal role in shaping the future of medicine. Within the academic sphere, Omar shines as an outstanding student, consistently surpassing his peers with his dedication and tireless effort. His commitment to excellence not only marks him as a future leader in medicine but also holds great promise for advancing the frontiers of healthcare.

STRATEGIES FOR THE PREVENTION OF HEREDITARY DISEASES IN A REPUBLIC OF TAJIKISTAN

NM Mamadshoeva[1,2], MD Kadamalieva[2], TI Subbotina[1], A Potapkina[1] and NA Zhuchenko[1]

[1]N.V. Sklifosovsky ICM, I.M. Sechenov First Moscow State Medical University, Russia
[2]Republican Medical Genetics Center Ministry of Health and Social Protection of the Population of the Republic of Tajikistan, Russia

Abstract:

In the past decades, genetic services have slowly become more integrated into healthcare of the Republic of Tajikistan. The region of Tajikistan may be affected to genetic diseases, this is due to the practice of consanguinity, which is culturally prevalent and the presence of isolated and semi-isolated populations. Numerous studies confirmed that on average each individual can be a carrier of several abnormal variants. The children of consanguineous unions have an increased risk of genetic disease due to an increased probability of expressing autosomal recessive gene mutations inherited from both parents. A high frequency of consanguineous marriages in Tajikistan has been reported in association with hereditary diseases of the neuromuscular system, hearing loss, complicated nephrolithiasis, and others. To develop a strategy for the prevention of hereditary diseases in Tajikistan, we conducted a pilot molecular genetic study of probands with suspected hereditary diseases and their families. Materials and methods: We examined 15 families (51 people) by NGS method. Blood samples from all patients and patients' family members were collected. Whole exome sequencing was performed at CENTOGENE (the rare disease company), all pathogenic variants were confirmed by the Sanger method. Results: 8 pathogenic variants in genes (*CYP21A2, AMER1, ALDH7A1, PQBP1, TGM1, DMD, FGFR3, PLP1*) were detected. In 11 cases the genetic diagnosis was confirmed, no clinically relevant variants, related to the described phenotype of probands in 4 families were identified. 6 autosomal recessive disorder (OMIM: 201910; 266100; 242300), 1 autosomal dominant (OMIM: 100800), 4 X-linked disorder (OMIM: 312080; 300373; 300463; 310200) were identified. In 10 cases, pathogenic variants were detected in the parents in heterozygous state or in the mother in heterozygous state, only the variant in the *FGFR3* gene was as the result of a de novo pathogenic variant. In the study consanguineous marriages (26%) were identified, marriage between cousins. At the same time, in families with consanguineous marriages, the pathogenic variant CYP21A2 c.293-13C>G was identified in all patients (age of probands from 2 to 4 years) and relatives (healthy carriers). Conclusion: A pilot study revealed rare hereditary diseases, the late age of diagnosis of hereditary metabolic disorders. For the prevention of hereditary diseases in a Republic of Tajikistan carrier detection, neonatal screening and genetic counselling programmes it is necessary to implement.

NEW MUTATION IN SERPING1 GENE C. 860 T>G IS A ASSOCIATED WITH C 1-INH -HAE TYPE 1

Lazarenko L[1,2], Sedykh A[1], Ostankova J[1], Savin T[1,2] and Totolian Ar[1,2]

[1]*Saint-Petersburg Pasteur Institute, Russia*
[2]*First Pavlov State Medical University of St. Petersburg, Russia*

Abstract:

Introduction: HAE is a rare disease with an autosomal dominant type of inheritance that affects approximately one in 50,000 people worldwide. HAE exhibits swelling in various parts of the body, which differs from histaminergic edema of 1-4 days in duration. These edema are dense to the touch, cause patients a feeling of soreness and bursting surrounding tissues. Edema are resistant to antihistamine therapy and are threatening when localized in the larynx, accompanied by abdominal attacks and often by specific dermatological phenomena called "marginal erythema". Such angioedema are unpredictable, appear after mechanical trauma and are associated with estrogen (menarche, pregnancy, contraception). HAE disrupts the quality of life of patients, accompanied by the development of depression and other disorders in the psycho-emotional sphere.

Materials: We investigated a family in Kronstadt, the town near Saint-Petersburg where the four generations suffered from angioedema, which lasted for several days, refractory to antihistamine drugs, accompanied with vomiting, abdominal attacks, marginal erythema. The true diagnosis has been unloaded for several decades. Routine analyses confirm the diagnosis of hereditary angioedema: low C4 complement fraction and C1 inhibitor (quantitative and functional). It was surprising, that we discovered unknown earlier mutation in gene SERPING1.

Methods: The patient's whole blood was the material. From the sample DNA was extracted using the test system «Ampley-Prime Ribo-Prep» (FBUN CNIUM). Nucleotide sequences of the exon SERPING1 gene were determined by directly sequencing Sanger fragments using ABIPRISM 3500(AppliedBiosystems,USA).

Results: Direct sequencing to confirm the diagnosis by Sanger of eight exons of the SERPING1 gene whose mutations are associated with development of hereditary angioedema. As a result of research in 5 gene exon SERPING1 was first identified as mutating c. 860 T>G in the heterozygous state. The mutation found results in the replacement of the amino acid leucine with arginine at 287 position in the SERPING1 protein.

Conclusion: Thus, the typical clinical picture of edema, hereditary aggravation, presence of laboratory parameters, indicating a decrease of C4 complement fraction, a decrease of C1 inhibitor (qualitatively and functionally) allow to diagnose hereditary angioedema. In this way we believe that we have a case with a new mutation in gene SERPING1 associated with hereditary angioedema.

Biography

Lazarenko Luidmila M.D, Ph.D, an expert in allergy and clinical immunology. She is a member of EAACI, BSACI, RAACI, an author of one patent and more than 50 articles, devoted in allergy and clinical immunology.

A NOVEL PENTAVALENT VACCINE CANDIDATE COMBINING OUTER MEMBRANE PROTEINS WITH CAPSULAR POLYSACCHARIDES COMPLETELY PROTECTS AGAINST ACINETOBACTER BAUMANNII

Ramadan Hassan, Yomna A Hagag, Heba Shehta Said and Hany I Kenawy
El-Mansoura University, Egypt

Abstract:

Acinetobacter baumannii is considered as one of the most virulent and infectious organisms that has an increased ability to both evade host immune response and resist various classes of antibiotics, leading to life-threatening infections. Multiple virulence factors have been implicated in the high prevalence rate of *A. baumannii* in hospitalized and immunocompromised patients. Moreover, improper use of antibiotics has led to the emergence of extensive drug resistant strains that urgently requires alternative strategies to control this superbug. Unfortunately, the availability of a licensed vaccine against *A. baumannii* infections is still challenged by the vast diversity among *A. baumannii* strains. Here, we report the development of a novel pentavalent vaccine candidate composed of two recombinant proteins (wza and yiaD) and a pool of capsular polysaccharides isolated from 3 clinical isolates. We tested this new vaccine *in vivo* in a mouse model of peritonitis against the standard strain ATCC 19606 in addition to 3 clinical isolates of *A. baumannii*. Immunization with this vaccine completely protected the challenged mice with 100% survival rate in case of all of the tested bacteria. Further clinical studies are urgently needed to evaluate the efficacy and safety of this proprietary vaccine to protect patients from *A. baumannii* lethal infections.

Biography

Ramadan Hassan have expertise in Immunology, Genetics, and molecular biology. He completed PhD from Genetic and Immunology Institute, Munich, Germany (1990). He has expertise in teaching as Head of Microbiology and Immunology Dept. El-Mansoura University. In addition, he has expertise as Head of Clinical Laboratory and Blood Bank of MCH, KSA for 10 years (1998 - 2008). Furthermore, he was a Chief of Infection Control and Quality Control of the Hospital (MCH). His opportunity was based on good evaluation of the systems and to create new pathways for improving healthcare. He has experiences in evaluation of research papers as a member of High Scientific Committee for the Promotion of professors and Assistant Professors of Microbiology and Immunology in Egypt (NO.13). He has built my experiences model after working years of in research, evaluation, teaching and administration both in hospital and education institutions.

INTEGRATION OF AI-BASED PHENOTYPING AND COMBINED GWAS REVEAL NOVEL GENETIC INSIGHTS OF IMAGE-BASED COMPLEX TRAITS WITH HUMAN FACE AS EXAMPLE

Xianjing Liu Z Xiong, M Kayser, EB Wolvius, F Liu, GV Roshchupkin
Erasmus MC University Medical Center, Netherlands

Abstract:

Genome-wide association study (GWAS) excel in identifying genetic links to phenotypes, but its application to complex image-based traits presents challenges, such as defining phenotypes which cover more variance of the image, and the need of sharing individual image data. Thus, we propose a pipeline merging AI-based image phenotyping and combine-GWAS techniques to analyze image phenotypes. Combine-GWAS introduces a powerful meta-analysis approach to enhance the relationship between phenotypes and genetic variants by integrating multiple phenotypes. Moreover, to handle multi-cohort collaborations without sharing data, we employ federated learning (FL). Our pipeline advances GWAS for image-based traits, as demonstrated with facial shape data.

Method: *Study population.* Two cohort were used to validate our FL framework: The children cohort (N=3,314) from the Generation R Study, mean age 10.4 +- SD 1.5; The elderly cohort (N=3,995) from the Rotterdam Study, mean age 69.6 +- SD 9.5.

Facial phenotyping. We used, previously developed, a 3D mesh auto-encoder, to compress the high-dimensional facial morphology into low-dimensional representations (i.e., endophenotypes). The auto-encoder were trained using FL open-source library NVIDIA Flare. Specifically, the parameters of auto-encoder were updated locally within each cohort, and were simultaneously shared across sites via internet. In this way, no raw image data were shared.

Afterwards, 200 facial endophenotypes derived from FL were used for GWAS.

GWAS. We performed single-trait GWAS using HASE framework to accelerate analysis, followed by EasyQC and the combine-GWAS for meta-analysis.

Results: After meta-analysis we found 43 independent significant SNPs, of which 12 were novel. Moreover, 43 facial heatmaps were displayed to visualize facial phenotypes associated with the 43 independent SNPs.

The identified SNPs are highly in line with existing studies. For example, rs4648379 (PRDM16) is known to be associated with the nose morphology; rs3122635(CRB1) is known to be associated with the chin dimples; rs752172 (PAX3) is known to be associated with nasal bridge. The GWAS catalog shows some of the identified SNPs were also reported in other studies such as asthma, insomnia, snoring, tooth development, brain/face morphology and total ventricular volume.

Conclusion: Our results demonstrate effectiveness of the proposed AI pipeline for sensitive medical image processing and follow-up genetic analysis. We expect the proposed pipeline can be an important tool for such genetics analysis within consortiums.

Biography

Xianjing Liu is a PhD researcher at the Biomedical Imaging Group Rotterdam (BIGR) at Erasmus MC under the supervision of Prof. Wiro J. Niessen, Prof. Eppo B. Wolvius, and Dr. Gennady V. Roshchupkin. Earlier, he has completed his Bachelors and Masters from Shenzhen University, and gained industrial experience as a R&D engineer at Shenzhen Wisonic Co., Ltd. and a researcher at Hong Kong Polytechnic University in collaboration with Esquel Group. At Erasmus MC, he primarily contributes to the 3D facial shape analysis project. His PhD research focuses on the interpretability and confounding problems in machine learning, with applications in medical studies.

STALIN BLACK DOGS: A POST MORTEM DIAGNOSIS

Pier Giorgio Righetti
Politecnico di Milano, Italy

Abstract:

I will describe here a modern and unique tool for exploring documents pertaining to the world Cultural Heritage while avoiding their contamination or damage. Known under the acronym EVA, it consists of a plastic foil of Ethylene Vinyl Acetate studded with strong cation and anion resins admixed with C8 and C18 hydrophobic beads. When applied to any surface such foils (cut into diskettes) can harvest any type of surface material, which is then eluted and analyzed via standard means, such as GS/MS (typically for metabolites), MS/MS (for peptide and protein analysis), X-ray (for elemental analysis). I shall review here a number of past data, such as screening of documents by Bulgakov, Chekov, Casanova, Kepler, as well as by Orwell and Stalin and analysis of the skin of an Egyptian mummy. As a unique example, I will quote here the analysis of a book Stalin was reading during World War II (Ivan Grozny): on the pages of this book we found plenty of lithium salts, suggesting that he was bipolar just like Winston Churchill This novel methodology represents a formidable tool for exploring the past life of famous authors, scientist and literates in that it can detect traces of their pathologies and even drug consumption left by saliva and sweat traces on their original hand-written documents. Prior to our invention, the only technique proposed was scraping or grating the surface of the material under investigation, clearly a technique strictly forbidden in museums, private and public collections. In the worst cases, when dealing with pottery or other clay material, chipping away of a piece was proposed, a barbarian way to treat items belonging to the Cultural Heritage.

SMOKING-ASSOCIATED CHANGES IN GENE EXPRESSION IN CORONARY ARTERY DISEASE PATIENTS USING MATCHED SAMPLES

Mohammed Merzah and Szilvia Fiatal
University of Debrecen, Hungary

Abstract:

Background: Smoking is a well-known risk factor for coronary artery disease (CAD). However, the effects of smoking on gene expression in the blood of CAD patients in Hungary have not been extensively studied.

Aim: To identify differentially expressed genes associated with smoking in coronary artery disease (CAD) patients.

Methods: Eleven matched samples based on age and gender were selected for analysis in this study. All patients were non-obese, non-alcoholic, non-diabetic, and non-hypertensive and had moderate to severe stenosis of one or more coronary arteries, confirmed by coronary angiography. Whole blood samples were collected using PAXgene tubes. Next-generation sequencing was employed using the NextSeq 500 system to generate high-throughput sequencing data for transcriptome profiling. The differentially expressed genes were analyzed using the R programming language.

Results: The median age of patients was 67 years (range: 54-75). RNA sequencing was performed on two groups: smokers and non-smokers. After quality control and filtering, gene expression data were obtained for all samples. Using DESeq2, we identified 279 differentially expressed genes with a p-value ≤ 0.05 and a log2 fold change ≥1. Of these genes, 160 were upregulated in the smokers, and 119 were downregulated compared to non-smokers. Gene ontology analysis revealed that the upregulated genes were enriched for pathways related to immune responses and activities (FDR< 0.03). Specifically, upregulated genes were involved in keratinocyte differentiation, cornification, and epidermis development. The downregulated genes were enriched for cell-cardiac muscle cell adhesion (FDR= 0.004) and epithelium development (FDR= 0.001) pathways.

Conclusion: This research sheds light on the complex biological effects of smoking and provides valuable insights into the mechanisms underlying smoking-related diseases. The findings also have implications for personalized medicine, where patients can be stratified based on their gene expression profiles to predict their risk of developing smoking-related diseases and tailor treatment plans accordingly.

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Accepted Abstracts

THE EFFECT OF POLYMORPHISMS CAUSING GLUTEN SENSITIVITY ON ORAL HEALTH

Cisem Silar
Marmara University, Turkey

Abstract:

Tooth enamel defects, oral burning, caries, etc. can be important effects of gluten sensitivity and celiac disease. Dentists also play an important role in diagnosing celiac and gluten sensitivity. Some of these oral manifestations are most likely due to nutritional deficiencies that are particularly common at the time of diagnosis, but they may also be related to salivary gland involvement. It is well known that saliva plays a very important role in maintaining oral health and that salivary gland dysfunction can lead to various oral diseases [1]. Tooth decay is a chronic infection caused by the normal oral microbial flora. There are millions of bacteria that make up the microbiota in the oral cavity. Some of these organisms initiate the formation of dental caries. Tooth decay is defined as the destruction and damage of the outer hard tissue of the tooth, the enamel layer, the dentin underneath, and sometimes the hard tissue covering the tooth root. Different genetic variations seen in different populations can affect both oral caries formation and oral microbiota and health. Interindividual variations in HLA molecules may explain differences in immune responses to microorganisms that affect susceptibility to oral diseases.

In our study, we aimed to examine the relationship between HLA-DQA1 and HLA-DQ8 gene polymorphisms, which are thought to be associated with gluten intolerance susceptibility, and caries formation, which is one of the oral health parameters. As a result of the literature readings, it has been determined that there is no current study examining the connection between these two gene regions of dental caries. The aim of our research is among the genes encoding the proteins involved in the immune system of our body; To determine whether there is a relationship between rs2187668 and rs7454108 polymorphisms in HLA-DQA1 and HLA-DQ8 genes, respectively, and dental caries, which is one of the main components of oral health. Genotyping studies will be performed using Real-Time PCR technique. The number of caries will be determined in the oral examinations of the participants; After the necessary genetic analyzes are made, the connection between them will be examined.

Acceleration of DNA methylation age as a biomarker for early onset of REM sleep behavior disorder

Ekaterina Rogaeva[1], Konstantin Senkevich[1,2], Amélie Pelletier[2], Christine Sato[1], Lang Liu[2], Allison Keil[2], Ziv Gan-Or[2,4], Anthony E. Lang[1,4] and Ronald Postuma[2,3,5]

[1]University of Toronto, Canada
[2]Mc Gill University, Canada
[3]Montreal Sacre Coeur Hospital, Canada
[4]Toronto Western Hospital, Canada
[5]The Research Institute of the McGill University Health Centre, Canada

Abstract:

REM sleep behavior disorder (RBD) is the strongest prodromal marker for α-synucleinopathies, such as Parkinson's disease, Lewy body dementia and multiple system atrophy. The Horvath DNA-methylation-age (DNAm-age) is an epigenetic clock reflecting biological aging. We found an association of DNAm-age-acceleration with RBD age-at-onset at baseline (N=162; P=2.59e-08) and follow-up (N=45; P=9.73e-06). The result remains highly significant after accounting for the effects of known genetic risk-factors (e.g., RBD polygenic risk score). RBD patients with faster epigenetic aging had 4.6 years earlier onset than patients with slow/normal aging. However, association with earlier age-at-phenoconversion did not reach statistical significance (N=53; P=0.06). Our findings suggest that acceleration of the epigenetic clock is a potential biomarker for earlier RBD onset, which unlocks the possibility for including it as an important predictor when designing a study or clinical trial (e.g., to estimate rate of disease progression and define cut-off points).

RARE RAS MUTATIONS ARE ASSOCIATED WITH RECURRENCE PATTERNS AND RECURRENCE-FREE SURVIVAL IN COLON CANCER: FIRST RESULTS FROM MOROCCO

El Agy Fatima
Sidi Mohamed Ben Abdellah University, Morocco

Abstract:

This exploratory study aimed to evaluate the impact of RAS mutations, especially the rare mutations type on recurrence patterns in patients with stage I-IV CRC, and to identify the risk factors predicting recurrence-free survival in colon cancer. Full RAS mutations were analyzed using Sanger and pyrosequencing for 270 patients. The MSI status was determined using immunohistochemical analysis. The correlation between Molecular alterations and recurrence patterns and recurrence-free survival was investigated. Statistical analysis was performed using the Kaplan–Meier method and the log-rank test. The mean patient's age was 55,4±14.7 with a moderate dominance of the male sex (n=146; 54.1%). The rate of recurrence after the first-line therapy was 31.5% (n=85). 13 (15,3%) patients had local recurrence, and 72 (84,7%) had distal recurrence. The most common distal recurrence site was the liver (n=34 ; 40,0%), followed by the lung (n=19 ; 22,4%). Of the 270 patients, 85 (31,5%) experienced recurrence, among whom 52,9% had mutant full RAS status, and 48,2% had KRAS mutations. Outside KRAS exon 2 mutations or rare mutations, were identified in 22 (8.1%) patients. The p.Q61L (Nras exon 3) mutation had the highest frequency in the rare mutation group (n=5 ; 22,7%), followed by the p.A146T (Kras exon4) variant (n=4 ; 18,2%). RAS mutation status, KRAS mutations, and rare mutations were more common in patients with lung recurrence. Rare mutation status was correlated with worse recurrence-free survival (p=0,001). Multivariate logistic regression analysis revealed that differentiation, perineural invasion, full RAS mutant status, and KRAS codon 12 mutations were independent factors for recurrence-free survival in colon cancer.

KERATIN-7 ANTISENSE IS A NOVEL AND HIGHLY EFFECTIVE STRATEGY TO SUPPRESS TUMORIGENESIS AND PROMOTE APOPTOSIS IN CASES OF BREAST CANCER

Hamed Hosseinalizadeh, Mohammad Rahmati and Mohamad Eftekhary
Guilan University of Medical Sciences, Iran

Abstract:

Expression of the keratin-7 (KRT7) is upregulated in breast cancer, and has been shown to correlate with cancer's poor prognosis; however, the precise mechanisms underlying its involvement in tumorigenesis and apoptosis are largely unexplored. In the present study, by using specific oligonucleotide antisense against KRT7, we investigated the in vitro effects of the knockdown of KRT7 on tumorigenesis and apoptosis of breast cancer cell lines. According to the results, antisense targeting KRT7 exerted a dose-dependent inhibitory effect on the viability of MDA-MB-468 and MCF-7 cell lines, whereas no cytotoxic effect was observed in normal cells. Our results suggest that KRT7 plays a significant role in directed migration, invasion, and proliferation during tumor growth, leading us to interpret that KRT7 is a metastasis-associated protein and has regulatory activity in EMT and subsequent cancer metastasis. In addition, our cellular studies showed that this approach resulted in a remarkable decrease in mammosphere formation (37% in mammosphere's number and 25% in size; in comparison to the control group of MDA-MB-468 and MCF-7 cells), as well as a decrease in cancer cells migration and an increase in cancer cell apoptosis (48% and 45%, respectively). Altogether, our findings have effectively established the involvement of KRT7 in the advancement of breast cancer through its regulation of the post-transcriptional sense mRNA.

Restoration of CD4+ T Cells during NAFLD without Modulation of the Hepatic Immunological Pattern Is Not Sufficient to Prevent HCC

Hussein Aqbi, Isbell M, Mirshahi F, Guo C, Saneshaw M, Koelsch N, Idowu MO, Austin D, Gelber C, Wang XY, Sanyal AJ and Manjili MH
University of Mustansiriyah, Iraq

Abstract:

Predominant inflammatory immunological patterns as well as the depletion of $CD4^+$ T cells during nonalcoholic fatty liver disease (NAFLD) are reported to be associated with the progression of hepatocellular carcinoma (HCC). Here, we report that an LRP-1 agonistic peptide, SP16, when administered during advanced NAFLD progression, restored the depleted $CD4^+$ T cell population but did not significantly affect the inflammatory immunological pattern. This data suggests that restoration of $CD4^+$ T cells without modulation of the hepatic immunological pattern is not sufficient to prevent HCC. However, SP16 administered early during NAFLD progression modulated the inflammatory profile. Future studies will determine if regulation of the inflammatory immune response by SP16 early in NAFLD progression will prevent HCC.

CARDIOMYOCYTE IL-1R2 PROTECTS HEART FROM ISCHEMIA/REPERFUSION INJURY BY ATTENUATING IL-17RA-MEDIATED CARDIOMYOCYTE APOPTOSIS

Jun Lin
Sun Yat-sen Memorial Hospital of Sun Yat-sen University, China

Abstract:

Myocardial ischemia reperfusion (I/R) injury is a complex process with intense inflammatory response and cardiomyocyte apoptosis. As a decoy receptor of IL-1β, Interleukin-1 receptor type 2 (IL-1R2) inhibits IL-1β signaling. However, its role in I/R injury remains unknown. Here we found that the serum levels of IL-1R2 were significantly increased in patients with acute myocardial infarction (AMI) following interventional therapy. Similarly, after myocardial I/R surgery, IL-1R2 expression was significantly increased in heart of wild-type mice. In addition, IL-1R2-deficient mice heart showed enlarged infarct size, increased cardiomyocyte apoptosis together with reduced cardiac systolic function. Following exposure to hypoxia and reoxygenation (H/R), neonatal rat ventricular myocytes (NRVM) significantly increased IL-1R2 expression relying on NF-κB activation. Consistently, IL-1R2-deficient mice increased immune cells infiltrating into heart after surgery, which was relevant with cardiac damage. Additionally, IL-1R2 overexpression in cardiomyocyte protected cardiomyocyte against apoptosis through reducing the IL-17RA expression both in vivo and in vitro. Our results indicate that IL-1R2 protects cardiomyocytes from apoptosis, which provides a therapeutic approach to turn down myocardial I/R injury.

EFFECT OF CUMINUM CYMINUM AND RHUS PENTAPHYLLA EXTRACTS ON STATUS EPILEPTICUS INDUCED BY INTRAHIPPOCAMPAL INJECTION OF KAINIC ACID IN RAT

Khadija Oubella
Cadi Ayyad University, Morocco

Abstract:

Our study aims to evaluate the anticonvulsant effect of the aqueous extract of Rhus pentaphylla and Cuminum cyminum (300 mg/kg), orally, 45 min before intrahippocampal injection of kainic acid (1 µg/µL). The scoring of seizure severity, latency of seizures and duration of total seizures were recorded in 90 min. Both extracts showed the presence of polyphenols, flavonoids, alkaloids and tannins compounds. These extracts exhibited potent antioxidant activity and showed an attenuation of severe convulsive seizures, a significant decrease in the frequency and duration of seizures and prolonged the latency of the onset seizure ($p<0.001$) compared to kainic acid. The aqueous extracts of R. pentaphylla and C. cyminum have a protective effect against seizures induced by kainic acid.

THE ROLE OF RARE VARIANTS IN THE DEVELOPMENT OF FAMILIAL PREMATURE CORONARY ARTERY DISEASE IN A COHORT OF IRANIAN PATIENTS

Kimia Kahrizi[1,6], Sepideh Mehvari[1], Nahid Karimian Fathi[1], Sara Saki[2], Maryam Asadnezhad[1], Sanaz Arzhangi[1], Fatemeh Ghodratpour[1], Marzieh Mohseni[1], Farzane Zare Ashrafi[1], Saeed Sadeghian[3], Mohammadali Boroumand[3], Fatemeh Shokohizadeh[3], Elham Rostami[3], Rahnama Boroumand[3], Reza Najafipour[1], Reza Malekzadeh[2], Yasser Riazalhosseini[5,6], Mark Lathrop[5,6], Mohammadreza Akbari[7,8], Hossein Najmabadi[1] and Kaveh Hosseini[3]

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Abstract:

Coronary artery disease (CAD), the most common form of cardiovascular diseases, is the leading cause of death globally. Heritable factors play an important role in the pathogenesis of CAD. Family history of such disease has long been recognized as a strong risk factor for CAD; approximately one-third of patients with CAD have a positive family history. In the present study, we aimed to identify potentially disease-causing rare variants in a cohort of 60 Iranian families with multiple affected individuals in several generations afflicted with established premature CAD (PCAD). Whole exome sequencing (WES) was performed for one or two patients of every family, followed by Sanger sequencing for confirmation of the results and co-segregation analysis. Subsequently, all available heterozygous, albeit seemingly healthy individuals underwent coronary computed tomography angiography (CCTA). In this study, likely causal rare heterozygous variants have been identified in seven genes, including *ABCG8, CD36, CYP27A1, PIK3C2G, RASSF9, RYR2* and *ZFYVE21*, showing co-segregation with familial PCAD in eight unrelated families. From among which, *PIK3C2G, RASSF9* and *ZFYVE21* are novel potential candidate CAD genes. Our findings indicate that rare variants in genes identified in this study would probably be involved in CAD development. However, further studies are needed to corroborate these results. In conclusion, identifying asymptomatic individuals at risk of CAD prior to disease onset could help to disease prevention and management.

COVID-19 IN A PRE-OMICRON ERA: A CROSS-SECTIONAL IMMUNO-EPIDEMICAL AND GENOMIC EVALUATION

Maryam Saud aljaid, Jorge Pamplona Pagnossa, Sarah de Oliveira Rodrigues, Gabriel Ferrari de Oliveira, Mohd Adnan, Maryam Saud Aljaid, Isabela Bacelar de Assis, Alex Sandro Gomes Lima, Mitesh Patel, Hanan A Ogaly and Gaber El-Saber Batiha

Taif university, Saudi Arabia

Abstract:

The seventh human coronavirus was discovered and reported primarily in Wuhan, China. After intense seasons with repercussions in all areas of humanity, the pandemic demonstrates a new perspective. In Brazil, the pandemic concept had impacts in vast areas, including healthcare hospitals. This present study aims to describe and synthesize data from a determined period from the year 2021 that correlate the symptoms of passive and/or active patients for COVID-19 and their respective results of IgG/IgM serological tests in hospitals in the city of Cruzeiro, São Paulo, Brazil. The form had been applied to 333 people and obtained conclusive results and several symptoms were presented; in addition, asymptomatic cases were also analyzed and directed in the genomic study of variants of concern, as well as vaccination data in the study region.

ENVIRONMENTAL AND GENETIC RISK FACTORS FOR TINNITUS AND HEARING LOSS

Natalia Yakimovska
Karolinska Institutet, Sweden
Shterev Hospital, Bulgaria

Abstract:

Tinnitus is a phantom auditory sensation, most often referred to as "ringing in the ears" with detrimental effect on quality of life. Between 4% and 37% of the global population has experienced tinnitus at some point in their life. For every 1 out of 10 individuals experiencing tinnitus, it becomes a severely impactful condition, affecting concentration, sleep, mood, and general quality of life. Despite its high prevalence and severe socio-economic burden, there is no successful treatment. The work presented in this thesis uses multiple scientific approaches to better understand the etiology of tinnitus, with the emphasis on the genetic landscape in order to gain insight into its molecular origins. First, we identify important gaps in knowledge on environmental risk factors associated with tinnitus. Second, we show using genetic epidemiology methods that severe tinnitus runs in families, which changes the current narrative that tinnitus would be generated purely due to environmental factors. Third, as tinnitus is commonly linked to hearing loss, we used a genome-wide biostatistical approach to reveal the genetic architecture of hearing loss, that will be further essential in distinguishing the two conditions. Fourth, we investigated the whole genome in relation to tinnitus to map correlated genomic regions and consequently, specific genes associated with tinnitus. Finally, we used a high-throughput sequencing of protein coding regions of the genome to identify disease-causing mutations impacting severe tinnitus. The work presented in this thesis provides insights from multiple aspects into the origins of tinnitus and will serve as a backbone to understanding the pathophysiology of the disorder.

ASSESSING HSA-MIR-19B-3P AS A POTENTIAL BIOMARKER FOR ASBESTOS AND RADON EXPOSURE

Rakhmetkazhy Bersimbaev and Olga Bulgakova
Institute of Cell Biology and Biotechnology, Eurasian National University, Kazakhstan

Abstract:

Background: MicroRNAs (miRNAs) are small non-coding RNA molecules that play important roles in the regulation of gene expression. They can post-transcriptionally modulate the expression of target genes by binding to specific messenger RNA (mRNA) molecules, leading to mRNA degradation or translational inhibition. miRNAs have been implicated in various cellular processes, including proliferation, development, differentiation, and cell death. miRNAs serve as promising biomarkers for a range of lung diseases, including lung cancer. According to the WHO, asbestos and radon are recognized as a carcinogens in the first category of the list of carcinogens. Exposure to asbestos fibers is strongly associated with the development of malignant mesothelioma and lung cancer. Prolonged exposure to radon causes damage of cellular components, mitochondria, and oxidative stress, which leads to damage of lung tissue. The study of miRNAs expression in response to asbestos and radon exposure is of particular interest due to the recognized carcinogenic properties of these substances, which elevate the risk of developing lung disease. miR-19b-3p is known to regulate genes involved in cell proliferation and apoptosis, two critical processes in cancer development.

Methods:A total of 269 subjects were examined, including: 62 healthy controls, 143 people working at an asbestos mining and processing facility and 64 individuals resided in areas with radon levels exceeding 100 Bq/m3. Blood samples were collected using tubes containing EDTA. The blood samples was centrifuged to separate the plasma which was stored at -80 0C. The level of miRNas was determined by qRT-PCR. 2x mercury SYBR Green Master Mix (#339346), primers (hsa-miR-19b-3p) and ROX dyes were used for the reaction mixture. Small nuclear RNA - U6 expression values were used as endogenous control. The relative expression levels of miRNAs were calculated using the $2-\Delta\Delta Ct$ methods for quantitative analysis.

Results: A study of the hsa-miR-19b-3p expression profile in individuals exposed and not exposed to asbestos revealed a significant reduction of this miRNA ($p<0.05$) in the group with occupational risk of chrysotile asbestos exposure. Opposite, the expression of hsa-miR-19b-3p was significantly increased in healthy individuals living in areas with high levels of radon compared to the control group ($p<0,05$). In our study, for the first time, we demonstrated changes in the expression level of hsa-miR-19b-3p in blood plasma following asbestos exposure. The differences we observed in the expression profiles of this miRNA following exposure to various carcinogens, leading to the development of lung cancer, offer significant prospects for using hsa-miR-19b-3p as biomarkers not only for lung cancer itself but also for its causes.

THE DIAGNOSTIC YIELD OF CGH AND WES IN NEURO DEVELOPMENTAL DISORDERS

Raniah S. Alotibi, Naif S. Sannan, Mariam AlEissa, Marwh G. Aldriwesh, Abeer Al Tuwaijri, Maaged A.Akiel, Mashael Almutairi , Alhanouf Alsamer , Nouf Altharawi, Ghadah Aljawfan, Badi Alotiabi,Mohammed A. AlBlawi and Ahmed Alfares

King Saud Bin Abdulaziz University For Health Sciences, Saudi Arabia

Abstract:

Background: Neurodevelopmental disorders are a group of conditions characterized by developmental delays leading to abnormal brain functions. The methods of diagnosis and treatment of these conditions are complicated, and their treatment involves a combination of various forms of therapy. In recent years, the development of high-resolution technologies has played an important role in revealing the microdeletions, microduplications, and single-nucleotide variants of the chromosomes and how they are linked to the development of neurodevelopmental disorders. The wide implementation and application of molecular methodologies have started to shed light on the functional importance of using the appropriate methods in detecting these genetic variations that are categorized as either pathogenic or benign. The study aimed to compare the diagnostic yield of comparative hybridization (CGH) and whole exome sequencing (WES) in neurodevelopmental disorders among children attending the King Abdullah Specialist Children Hospital, Riyadh, Saudi Arabia.

Methods: A retrospective study was conducted between 2015 and 2018 on 105 patients diagnosed with neurodevelopmental disorders through array-based CGH (Array-CGH) and WES.

Results: In a sample of 105 patients, 16% was the hit rate of copy number variations (CNVs). WES was requested for CNV-negative patients (n = 79), of which 30% was the hit rate of pathogenic or likely pathogenic single-nucleotide variants. There was a difference in the diagnostic yield between CGH (16%) and WES (30%).

Conclusion: WES was a better approach than Array-CGH to detect various DNA mutations or variants. Our findings could guide clinicians, researchers, and testing laboratories select the most cost-effective and appropriate approach for diagnosing their patients.

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