

Meeting Abstracts

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Meeting abstracts of 3rd European Congress on Human Genetics

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1. THE ROLE OF NUTRIGENETICS AND EPIGENETICS IN LONGEVITY: HOW CAN WE TURN BACK OUR EPIGENETIC CLOCK?

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Understanding the biological mechanisms of healthy aging has become increasingly important. It is necessary to understand epigenetic mechanisms to prevent epigenetic diseases such as allergies, autoimmune diseases, neurodegenerative diseases, cardiovascular diseases, and cancer. Aging is a systemic process that affects all biological systems and is characterized by an increasing frequency of age-related degenerative diseases. The epigenetic clock uses DNA methylation patterns to estimate biological age and monitor the aging process. A healthy lifestyle helps align biological and chronological ages, but environmental factors can disrupt this balance. Regular monitoring of the epigenetic clock allows researchers to evaluate the effectiveness of dietary and lifestyle interventions. Nutrigenetic analysis has emerged as a valuable tool in studying the interaction between nutrition and genetics. Genetic factors can affect the absorption, metabolism, and utilization of various nutrients. Nutrigenetic analysis helps provide personalized dietary recommendations based on genetic profiles and reduces the risk of nutrient deficiencies. Anti-aging encompasses a range of interventions aimed at slowing or reversing the effects of



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aging. These strategies usually include biochemical, lifestyle, and in some cases genetic interventions. Combining nutrigenetic analysis with epigenetic clock data offers a comprehensive approach to support healthy aging and longevity.

2. PRECISION DISEASE MODELING FOR TRANSLATIONAL GENETICS

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Rare diseases encompass more than 8,000 distinct conditions, the majority of which lack effective treatments. Advances in sequencing technologies have revolutionized the identification of genetic variants underlying these diseases, providing valuable insights into potential therapeutic targets. However, significant challenges remain. First, determining the pathogenicity of identified variants is often difficult. Second, even when a disease-causing variant is confirmed, developing targeted therapies requires precise disease models that replicate the specific genetic variants in the relevant organs or tissues affected in patients. To address these challenges, we have pioneered a novel “Gene Replacement” approach using *Drosophila* as a model system. This strategy enables detailed functional studies of genetic variants and the creation of precision disease models tailored for therapeutic development. Applying this approach, we have successfully validated numerous disease-causing variants identified in patients with heart and kidney disorders. Furthermore, these precision disease models have been instrumental in uncovering disease mechanisms and guiding the development and testing of mechanism-based therapeutic treatments. By bridging the gap between genetic discovery and therapeutic application, the “Gene Replacement” approach establishes a transformative platform for translational genetics, with the potential to improve the lives of millions of patients affected by rare diseases worldwide.

3. BLOOD RHEOLOGY AND SIMILARITY TO AN ENGINEERING SUSPENSION

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Human blood is a mixture of liquid and solid phases. The liquid phase, called plasma, constitutes about 55% of the volume of whole blood, while the remaining 45% consists of cellular elements. Plasma serves as a carrier for these cellular elements, and it is composed of about 90% water. Approximately 99% of all cellular elements belong to red blood cells. Whole blood has a complex structure and demonstrates a non-linear dependence of shear rate on shear stress. In addition, blood exhibits a yield stress that depends on the concentration of red blood cells. An engineering suspension, which demonstrates similarities to blood, will be presented. Both blood and the chosen engineering suspension have solid particles of comparable size and shape that tend to form rouleaux at low shear rates, leading to increased yield stress and viscosity. It will be shown that red blood cells and solid particles in the engineering suspension significantly contribute to viscosity and yield stress. Measurements of blood flow properties such as wall shear stress and velocity profiles are extremely difficult; therefore, the latest measurement technologies and alternative approaches to mathematical modeling of blood and engineering suspension flow will be presented and discussed. The phenomenon of turbulence damping during blood and engineering suspension flow will also be demonstrated. The objective of this study is to illustrate human blood rheology by presenting experimental results for different concentrations of red blood cells and to emphasize the similarity to an engineering

suspension with respect to energy losses during flow. The results are presented in graphs, and conclusions will be drawn.

4. REVOLUTIONIZING HEREDITARY TUMOR SYNDROME DIAGNOSIS: ADVANCED GENOMIC TECHNOLOGIES REVEAL HIDDEN GENETIC VARIANTS AND ENHANCE PATIENT CARE

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Advanced diagnostic techniques have significantly improved the detection and characterization of genetic disorders, particularly in patients who test negative with standard diagnostic methods. This study focuses on the application of advanced genomic technologies to enhance the diagnosis of neurofibromatosis type 1 (NF1)/schwannomatosis and the identification of driver variants in somatic tissues. We analyzed a cohort of 89 patients with complete clinical profiles and negative next-generation sequencing (NGS) results, utilizing RNA sequencing (RNA-Seq), ultra-deep sequencing, and nanopore long-read sequencing. RNA-Seq was performed using the TruSight RNA Pan-Cancer Panel targeting 1,385 cancer genes, while ultra-deep sequencing employed the SureSelect XT HS2 Target probes for genes such as *LZTR1*, *SMARCB1*, *NF1*, and *NF2*. Our findings revealed that integrating RNA-Seq and ultra-deep sequencing significantly increased the diagnostic yield. In patients with segmental or mosaic NF1 who presented with clinical features localized to specific body regions, cell-free DNA (cfDNA) ultra-deep amplicon sequencing enabled the detection of pathogenic variants at very low frequencies. This approach was particularly effective in identifying deep intronic variants and structural rearrangements typically missed by conventional DNA-based tests. Additionally, whole-exome sequencing (WES) of somatic biopsy samples from benign plexiform neurofibromas (PNs) and malignant peripheral nerve sheath tumors (MPNSTs) within the same patient identified novel genetic driver mutations associated with malignant transformation. The study also employed DNA methylation epigenomes to characterize different tumor stages and malignancy, providing a non-invasive prognostic tool for early detection of circulating tumor DNA (ctDNA) in plasma samples. Overall, the implementation of these advanced diagnostic technologies offers a comprehensive approach to improving genetic diagnosis and monitoring disease progression in NF1 patients, ultimately contributing to personalized treatment strategies and improved clinical outcomes.

5. SENESCENT ENDOTHELIAL CELLS PROMOTE LIVER METASTASIS OF UVEAL MELANOMA IN SINGLE-CELL RESOLUTION

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Background: Uveal melanoma (UM), the most common adult intraocular tumor, is characterized by high malignancy and poor prognosis in advanced stages. Angiogenesis is critical for UM development; however, the role of vascular endothelial dysfunction in UM remains unclear, and single-cell level analyses have been lacking. A comprehensive investigation is essential to clarify the contribution of the endothelium to UM progression.

Methods: Using single-cell RNA transcriptomics data from 11 cases of primary and liver metastatic UM, we analyzed endothelial cell (EC) status. ECs were further analyzed and validated using *in vitro* models and clinical specimens. We then investigated the impact of endothelial dysfunction on UM cell migration and explored the mechanisms underlying EC abnormalities and their peripheral effects.

Results: UM metastases contained a significantly higher proportion of vascular endothelial cells compared with primary tumors, and ECs in metastases exhibited pronounced senescence. Senescent ECs showed strong upregulation of Krüppel-like factor 4 (KLF4). Overexpression of KLF4 in normal ECs induced senescence, whereas knockdown of KLF4 in senescent ECs inhibited senescence, identifying KLF4 as a driver gene of endothelial senescence. KLF4-induced EC senescence promoted tumor cell migration through a senescence-associated secretory phenotype (SASP). Among SASP components, C-X-C motif chemokine ligand 12 (CXCL12) was identified as a key effector, contributing to the formation of an immunosuppressive microenvironment.

Conclusion: This study reveals the pro-metastatic role of senescent endothelial cells in UM, highlighting KLF4-driven endothelial senescence and SASP/CXCL12 signaling as potential therapeutic targets.

6. HOW ACUPUNCTURE MODIFIES EPIGENETIC EXPRESSION IN FIBROMYALGIA: A PATH TO PERSONALIZED THERAPY

Hicran USAN

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Fibromyalgia (FM) is a complex, chronic pain disorder characterized by widespread musculoskeletal pain, fatigue, sleep disturbances, and cognitive impairment. While its precise etiology remains unclear, recent research has highlighted epigenetic modifications as key contributors to its pathophysiology. Epigenetic mechanisms - including DNA methylation, histone modifications, and non-coding RNA activity - regulate gene expression without altering the genetic code, thereby influencing how environmental and lifestyle factors drive disease onset and progression. Acupuncture, a fundamental practice in traditional Chinese medicine, has gained increasing recognition for its role in managing FM symptoms. Emerging evidence suggests that acupuncture modulates epigenetic processes, potentially reversing maladaptive gene expression patterns associated with chronic pain and neuroinflammation. Studies indicate that acupuncture may restore homeostasis by regulating DNA methylation in genes linked to central sensitization, stress responses, and neurotransmitter balance, thereby offering long-term symptomatic relief. Additionally, acupuncture has been shown to influence histone acetylation, affecting chromatin remodeling and the transcriptional activation of anti-inflammatory and neuroprotective genes. By modifying histone structures, acupuncture may mitigate neuroinflammatory responses and promote autonomic nervous system stability. Moreover, microRNAs (miRNAs) - small non-coding RNAs that regulate gene expression post-transcriptionally - have been implicated in acupuncture-induced analgesia. Recent findings suggest that acupuncture modulates specific miRNAs involved in pain processing, neuronal plasticity, and immune responses, further supporting its role as an epigenetic modulator. Beyond molecular-level changes, acupuncture provides clinical benefits by improving pain thresholds, reducing fatigue, enhancing sleep quality, and alleviating mood disturbances commonly associated with FM. Integrating acupuncture into FM treatment protocols could facilitate a more personalized and targeted therapeutic approach, reducing reliance on pharmacological interventions and their associated side effects. This presentation will explore the intricate relationship between epigenetics and acupuncture in FM management. By examining recent

scientific advances, we aim to elucidate how acupuncture-induced epigenetic modifications contribute to sustained pain relief and symptom control. Understanding these mechanisms could pave the way for personalized FM therapies, leveraging epigenetic insights to optimize acupuncture's efficacy in individualized treatment plans. Future research directions and potential clinical applications in precision medicine will also be discussed.

7. GENETIC RELATIONSHIP OF ATTENTION DEFICIT AND HYPERACTIVITY DISORDER AND EFFECT OF EPIGENETIC FACTORS ON TREATMENT

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Long-term studies on Attention Deficit and Hyperactivity Disorder (ADHD) have shown that the heritability of this condition is as high as 74%, with approximately one-third of the heritability attributed to a polygenic component consisting of numerous common variants, each exerting small effects. This has made genetic factors a central focus in efforts to understand the etiology of ADHD. ADHD is a neurodevelopmental disorder that typically begins in childhood, characterized by symptoms of inattention, impulsivity, and hyperactivity. Its prevalence, which remains relatively stable across different geographic and cultural contexts, affects about 5% of children and frequently co-occurs with mood, anxiety, behavioral, learning, and substance use disorders. Importantly, studies indicate that two-thirds of children with ADHD continue to experience persistent symptoms into adulthood. Building on this knowledge, a case report was prepared on identical twins with ADHD, allowing for an evaluation of pathogenesis in individuals with the same genetic background but differing environmental exposures and nutritional habits since adolescence. Epigenetic modifications, influenced by factors such as environmental conditions, diet, chemical exposures, radiation, and comorbid diseases, were examined. Remarkably, identical twins with ADHD who adopted different lifestyles and nutritional strategies demonstrated a 36% improvement in the disease's pathogenesis, positively influencing both social behavior and overall lifestyle. These findings suggest that favorable epigenetic changes may reduce the heritability impact of ADHD in subsequent generations. This article, therefore, reviews the role of genes in the etiology of ADHD from two complementary perspectives: the molecular genetics view, which elucidates how genes influence biological pathways leading to ADHD, and the epigenetic perspective, which highlights the potential to alter the course of genetic transmission - and thereby reduce the incidence of ADHD in the population - through appropriate environmental and nutritional interventions.

8. PRIMATE-SPECIFIC HERVH ENHANCER NETWORKS SAFEGUARD GENOME INTEGRITY AND GERMLINE COMPETENCE IN EARLY HUMAN DEVELOPMENT

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Transposable elements (TEs) strongly influence genome stability during pre-implantation development and are often highly expressed in pluripotent and germ cells, potentially driving the rapid evolution of these stages. While active TEs can disrupt genomic integrity through new insertions, co-opted, transposition-incompetent TEs may contribute to stability by acting as regulatory elements. Germ cells are particularly vulnerable to genomic damage and therefore require robust protective mechanisms. Endogenous

retroviruses (ERVs), ancient viral integrations that entered host genomes via germline insertions, can remain active in both somatic and germline lineages. In mammals, pluripotency and germline development are closely interconnected: post-implantation epiblast cells give rise to primordial germ cells (PGCs), which reacquire pluripotent characteristics. PGCs and pluripotent stem cells (PSCs) share transcription factors (TFs), reflecting overlapping regulatory networks. The primate-specific ERV HERVH, the most abundant proviral sequence in the human genome, integrated into our lineage over 40 million years ago and was inactivated around 35 MYA. In human pluripotent cells, LTR7-driven HERVH elements reshaped transcriptional regulation by providing enhancers, alternative promoters, new exons, and chromatin boundaries. These elements suppress mutagenic TEs, promote self-renewal and pluripotency, and precisely mark embryo-contributing cells (eFORM). Functioning as enhancer hubs, LTR7-HERVH loci recruit core pluripotency TFs such as OCT4, NANOG, and KLF4, while also being enriched for PGC-specification factors including GATA-TFs, BLIMP1, and SOX17, suggesting a role in germline identity. To test this, we used CRISPR-Cas9 to delete selected HERVH copies in human embryonic stem cells (hESCs) and differentiated them into PGC-like cells (PGCLCs). Our results demonstrate that LTR7-HERVH-based enhancer networks act as super-enhancers linking pluripotent and germline states. Distinct HERVH loci exhibit stage-specific activity during PGC development, indicating dynamic roles in coordinating cell identity. Disruption of HERVH regulation impairs PGCLC differentiation and compromises TE repression, underscoring its essential role in maintaining germline competence and genome stability. Collectively, these findings highlight how LTR7-HERVH contributes to early human development and safeguards the emerging germline against genomic instability.

9. OBESITY-GENE RELATIONSHIP AND NUTRIGENETIC APPROACH

Esra Şahin

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In today's world, the interaction between lifestyle and genetics has emerged as a critical determinant of metabolic health, with obesity representing one of the most significant consequences of this imbalance. Conventional dietary programs often produce variable results across individuals, highlighting the importance of nutrigenetics, a field that develops personalized nutrition plans based on genetic profiles to optimize weight control and metabolic outcomes. Key genes involved in appetite regulation, fat metabolism, and weight management include *FTO*, *LEP*, and *LEPR*. Polymorphisms in the *FTO* gene increase the propensity for fat storage and energy intake, thereby elevating obesity risk. Similarly, alterations in the *LEP* gene can disrupt leptin signaling or cause leptin deficiency, leading to heightened appetite, weight gain, and metabolic dysfunction. Notably, the *LEP* rs7799039 variant, particularly the G allele, has been associated with increased anthropometric measures and a higher risk of obesity. Furthermore, individuals with *LEPR* gene variations may have impaired satiety perception, predisposing them to overeating and weight gain. Nutrigenetic analyses provide a framework for designing personalized dietary and supplementation strategies that account for such genetic differences, thereby enhancing the effectiveness of nutritional interventions. By aligning dietary approaches with individual genetic predispositions, nutrigenetics enables long-term metabolic regulation, improved weight management, and reduced obesity risk. As advances in this field expand, gene-based nutrition promises to transform health management strategies, promoting tailored, sustainable, and effective interventions for obesity and related metabolic disorders.

10. COMBINING PATIENT-DERIVED ORGANOID WITH COMPUTATIONAL MODELING TO STUDY METABOLIC-ASSOCIATED FATTY LIVER DISEASE PROGRESSION

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Background and Aims: Fatty liver disease is a growing global health burden, currently affecting more than 25% of the population worldwide. This study characterizes advanced patient-derived organoids generated from tissues of individuals diagnosed as healthy, with metabolic-associated fatty liver disease (MASLD), metabolic-associated steatohepatitis (MASH), or MASH cirrhosis. A computational modeling framework was applied to elucidate and predict the fundamental metabolic alterations underlying MASLD progression.

Methods: Patient-derived liver organoids were established using standardized protocols with informed consent. Tissue samples were enzymatically digested, and the resulting cells were cultured in a three-dimensional extracellular matrix (Geltrex) for at least one week. Organoid growth kinetics and morphology were monitored, and patients were stratified into three cohorts: healthy controls, MASLD/MASH, and cirrhosis. Computational models were applied to capture proliferation, cell death, and growth kinetics. Multiplex immunohistochemistry provided data on proliferation rates, apoptosis, and cell-cell interactions. Organoids were further classified using antibody markers including KI67, HNF4, Albumin, γ H2AX, CK19, and LGR5, enabling assessment of their cellular composition. Comparative analyses across cohorts were integrated into the computational framework.

Results: Organoids were successfully derived from all patient categories, exhibiting distinct growth kinetics and morphological features. Multiplex analysis confirmed lineage-specific differences, with variations in proliferative and functional markers across disease stages. Integration of experimental data with computational models revealed time-dependent growth dynamics and highlighted stage-specific regulatory mechanisms associated with MASLD progression.

Conclusion: This study demonstrates that combining patient-derived organoids with computational modeling enables precise evaluation of growth kinetics and cellular composition in MASLD, MASH, and cirrhosis. The findings underscore individualized disease patterns and provide a predictive framework for metabolic alterations, highlighting the potential of this integrated approach to advance organoid-based liver disease research and therapeutic development.

11. MANAGING GENE THERAPY REGULATIONS IN HUNGARY: ALIGNING TECHNOLOGICAL ADVANCES WITH LEGAL STANDARDS

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This paper examines how modern gene therapies, particularly those utilizing CRISPR technologies, can be integrated into Hungary's legal framework within the broader context of European Union regulations. The complex interplay of EU directives and Hungarian national laws creates a unique regulatory landscape for these advanced therapeutic interventions. The research focuses on the ethical challenges faced by regulators, such as privacy concerns, genetic discrimination, and informed consent. Furthermore, it explores the societal implications of these technologies, including issues of accessibility and public perception. The goal is to provide comprehensive insights that may guide policy adjustments and foster a regulatory

environment conducive to scientific innovation while ensuring ethical integrity and maintaining public trust in gene therapy advancements.

12. ADVANCES IN THE STUDY OF HEMOGLOBINOPATHIES AND OTHER ANEMIAS IN THE DOMINICAN REPUBLIC

Aide Rosa E. Cornielle-Dipre, Altagracia A. Hernandez, Maria Ramona Alberto, Maximo Santana, Carmen Sierra, Reyna Soriano, Biannely Cabrera, Sandra Sang, Marcos Cabrera, Jhoanny Batista, Jessica Encarnacion, Emely Feliz, Nathaly Baez

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Anemia is a serious public health problem with global impact. This condition is characterized by a deficit in the supply of oxygen to the body, generally due to an insufficient number of red blood cells in circulation. Anemia is caused by multiple factors, including iron deficiency, bleeding, hemoglobinopathies, and others. Hemoglobinopathies encompass a significant group of alterations in hemoglobin, the protein present in red blood cells responsible for oxygen transport. Most hemoglobinopathies are inherited in an autosomal recessive manner. These alterations can be structural, as in sickle cell anemia, or due to a deficiency in the synthesis of one of the globin chains, as in thalassemias. Our work aims to present the progress of a descriptive, prospective, cross-sectional study documenting the presence of various hemoglobinopathies and their possible interactions with each other and with other anemias in two populations of the Dominican Republic, located on the island of Hispaniola in the Caribbean Sea. The study participants were 48 secondary school students, aged 15-18 years, from the provinces of Barahona and Santo Domingo, located in the southwest and southeast of the Dominican Republic (DR), respectively. The methods and techniques included screening for microcytosis and/or hypochromia using a complete blood count (KN-21X, Sysmex), alkaline hemoglobin electrophoresis (Interlab G-26), and capillary electrophoresis; iron profile assessment included transferrin, transferrin saturation, ferritin, serum iron, iron percentage, TIBC, and UIBC (A-15 Biosystems). The overall prevalence of hemoglobinopathies and iron deficiency was 18.7%:12.5% were hemoglobinopathies (6.25% structural hemoglobinopathies - Hb AS and Hb AC traits; 4.2% suspected beta-thalassemia trait; 2.05% interactions between alpha-thalassemia trait and sickle cell trait (Hb AS)); 4.16% were due to iron deficiency, and 2.08% involved interactions between sickle cell trait (Hb AS) and iron deficiency. Positive cases from Barahona province had a higher percentage of hemoglobinopathies (67%) compared to those from Santo Domingo (33%). These results demonstrate the heterogeneity of the genotypic and phenotypic diversity of hemoglobins in the southeastern and southwestern regions of the DR, as well as the potential implications for the diagnosis and management of anemia.

13. ADAMTS13 GENE POLYMORPHISMS AND CORONARY ARTERY DISEASE RISK, PATIENT SURVIVAL, AND CLINICAL PHENOTYPE

Justyna Wrona, Anna Balcerzyk-Matić, Alicja Jarosz, Tomasz Nowak, Tomasz Iwanicki, Katarzyna Mizia-Steć, Paweł Bańka, Artur Filipecki, Katarzyna Gawron, Jolanta Krauze, Paweł Niemiec

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Introduction: ADAMTS13 (A Disintegrin-like And Metalloprotease with Thrombospondin motifs 13) is commonly referred to as the von Willebrand factor (vWF)-cleaving protein. vWF is a multimeric glycoprotein that mediates platelet adhesion to the endothelial layer of blood vessels during vessel wall

injury. By cleaving von Willebrand factor multimers, ADAMTS13 reduces platelet adhesion and aggregation, regulates thrombus formation, and inhibits inflammation. Patients with coronary artery disease (CAD) have lower ADAMTS13 antigen levels, and an early decline in ADAMTS13 is a significant predictor of future thrombotic events. ADAMTS13 expression may be affected by variability in the ADAMTS13 gene; therefore, in the current study, we analyzed the influence of ADAMTS13 polymorphisms on the risk of CAD, patient survival, and clinical phenotype.

Methods: The study group included 260 patients diagnosed with CAD and 237 control blood donors. Genotyping of ADAMTS13 single nucleotide polymorphisms (SNPs), i.e., rs2301612, rs2073932, and rs2285489, was performed using TaqMan-PCR.

Results: Polymorphisms of the ADAMTS13 gene showed no statistically significant association with the risk of CAD or patient survival at 5- and 10-year follow-up. However, carrying the A allele (rs2073932) was associated with left ventricular hypertrophy ($P = 0.048$), while carrying the G allele (rs2301612) was associated with the occurrence of ischemic stroke ($P = 0.010$). In addition, carriers of the G allele (rs2073932) had lower HDL levels ($P = 0.022$), and carriers of the C allele (rs2285489) had increased total cholesterol levels ($P = 0.025$).

Discussion: ADAMTS13 gene polymorphisms are associated with the clinical phenotype of CAD, including left ventricular hypertrophy, ischemic stroke occurrence, and blood lipid levels. However, their impact on the risk of CAD or patient survival has not been demonstrated in Polish CAD patients. The results of the current study may reflect the effect of these polymorphisms on ADAMTS13 levels and activity. Additionally, an *in-silico* study indicates that rs2285489 is associated with ADAMTS13 expression in the aorta, while rs2073932 is associated with gene expression in the coronary arteries. Due to limited knowledge, further research is needed to investigate the involvement of the ADAMTS13 gene in the development of coronary heart disease.

14. CYTOTOXIC PEPTIDE@NANOPARTICLE: A BIOMIMETIC STRATEGY TO REACTIVATE APOPTOSIS IN TUMOR CELLS

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Apoptosis, or programmed cell death, is a fundamental process in maintaining homeostasis in multicellular organisms. In cancer cells, apoptosis is often inhibited by apoptosis-inhibiting proteins (IAPs), whereas in healthy cells, IAPs are inhibited by Smac/DIABLO, a mitochondrial protein that promotes apoptosis. Elevated levels of IAPs in cancer cells contribute to cell survival, disease progression, chemoresistance, and poor prognosis.

In this study, we describe the preparation and *in vitro* validation of a synthetic Smac/DIABLO mimetic, based on fluorescent periodic mesoporous organosilicate (PMO) nanoparticles carrying Smac/DIABLO linked to a tumor integrin peptide ligand. At low micromolar concentrations, the biomimetic exhibited significant toxicity toward tumor cells, with only modest toxicity toward other integrin-expressing cells. This biomimetic demonstrated a strong ability to reactivate apoptosis and overcome acquired resistance following treatment with chemotherapy drugs.

15. THE ROLE OF SUCRASE-ISOMALTASE GENE VARIANTS IN IRRITABLE BOWEL SYNDROME

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Irritable bowel syndrome (IBS) is a complex gastrointestinal disorder characterized by chronic abdominal discomfort, bloating, and altered bowel habits. Recent advances suggest that sucrase-isomaltase (SI), an enzyme critical for digesting sucrose and starches in the small intestine, plays a key role in IBS pathophysiology. SI enzymatic activity accounts for approximately 60%-80% of starch digestion, while the remaining portion is managed by maltase-glucoamylase. Genetic variations in the SI gene, such as rs9290264 (Val15Phe), rs9283633 (Thr231Ala), and rs4855271 (Met1523Ile), have been associated with impaired enzymatic function, resulting in maldigestion and colonic fermentation of undigested carbohydrates. This process can exacerbate common IBS symptoms, including diarrhea, bloating, and abdominal pain, particularly in diarrhea-predominant (IBS-D) and mixed (IBS-M) subtypes.

Diagnosis and management of IBS are often challenging due to its heterogeneous nature and reliance on symptomatic treatments. Conventional approaches, such as the low-FODMAP diet, provide symptom relief for some patients but are highly restrictive and difficult to sustain. In contrast, emerging evidence suggests that patients with SI-related enzyme deficiencies respond better to personalized dietary interventions specifically targeting sucrose and starch intake. These tailored strategies are less restrictive, more practical, and offer superior symptom control, improving patients' quality of life.

The potential role of SI in IBS underscores the need to integrate genetic insights into clinical practice. By identifying genetic variants that impair SI function, healthcare providers can design targeted and sustainable dietary plans, reducing both patient burden and healthcare costs. This personalized approach represents a promising avenue for optimizing IBS management and advancing our understanding of its pathophysiology.

16. THE IMPORTANCE OF NUTRIGENETICS-BASED DIET IN PRECISION MEDICINE

Neval Burkay

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Precision medicine refers to an approach that emphasizes individualized preventive or therapeutic medical interventions, which are considered more effective than “one-size-fits-all” healthcare strategies. This approach aims to provide “the right treatment, to the right person, at the right time” by incorporating an individual's genetic characteristics, lifestyle, and environmental factors into medical treatment and prevention strategies.

Nutrigenetics is a scientific field that examines genetic differences influencing individuals' responses to diets. Single nucleotide polymorphisms (SNPs), which cause genetic variations, contribute to the diversity in dietary responses among individuals. The goal of nutrigenetics-based nutrition is to create personalized diet plans tailored to an individual's genetic characteristics. For example, caffeine metabolism varies based on the CYP1A2 gene. Fast metabolizers with the CYP1A2 1A variant can tolerate higher caffeine intake, while slow metabolizers with the CYP1A2 1F variant may experience side effects such as increased heart rate,

making it beneficial for them to limit caffeine consumption.

Similarly, histamine intolerance is associated with AOC1 gene variations that reduce the activity of the DAO enzyme, leading to symptoms such as headaches, flushing, and gastrointestinal discomfort after consuming histamine-rich foods. A low-histamine diet and DAO supplements can help manage these symptoms. Lactose intolerance results from variations in the LCT gene, leading to decreased lactase production and symptoms like bloating and diarrhea. A lactose-free diet or lactase supplements are effective in managing these symptoms.

By analyzing an individual's genetic profile, healthcare professionals can offer tailored advice on nutrients, dietary patterns, and supplements. This approach not only enhances the effectiveness of dietary interventions but also minimizes the risk of adverse reactions and unnecessary supplementation. As nutrigenetics continues to advance, the identification and understanding of SNPs will play a key role in advancing precision medicine and promoting optimal health through personalized nutrition.

17. ARTIFICIAL INTELLIGENCE IN PERSONALIZED MEDICINE: TRANSFORMING GENETICS AND EPIGENETICS FOR PRECISION HEALTHCARE

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The advent of Artificial Intelligence (AI) has revolutionized personalized medicine, particularly in the fields of genetics and epigenetics. AI algorithms, powered by machine learning (ML) and deep learning (DL) techniques, are now capable of processing vast datasets derived from genomic sequencing, epigenomic profiling, and multi-omics analyses. This presentation explores the transformative impact of AI in decoding complex biological networks to facilitate precision diagnostics, prognostics, and therapeutic interventions.

In genetics, AI enhances variant calling, interpretation of single nucleotide polymorphisms (SNPs), and the identification of rare genetic mutations with clinical significance. Deep neural networks (DNNs) have demonstrated high accuracy in predicting gene-disease associations and identifying potential drug targets. In epigenetics, AI models are instrumental in analyzing DNA methylation patterns, histone modifications, and non-coding RNA activities, offering insights into gene regulatory mechanisms and their implications in disease progression.

Furthermore, AI-driven integrative frameworks can model gene-environment interactions, aiding the development of personalized treatment plans. Techniques such as reinforcement learning and generative adversarial networks (GANs) are being employed to predict patient-specific responses to drugs, optimize clinical trial designs, and accelerate drug discovery.

This presentation aims to provide a comprehensive overview of current AI methodologies in personalized medicine, with case studies highlighting real-world applications. It will also address challenges such as data heterogeneity, model interpretability, and ethical considerations in clinical genomics. By leveraging AI's potential, we move closer to realizing truly personalized healthcare strategies.

18. VECTORS OF CHANGE: SHAPING THE NEUROMUSCULAR FUTURE THROUGH AAV9-MEDIATED GENE THERAPY

Esra Yayla

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Neuromuscular diseases, such as Duchenne muscular dystrophy (DMD), are conditions that not only affect the muscles but also involve multiple systems within the human body, significantly impairing quality of life. The majority of clinical treatments primarily focus on alleviating symptoms and prolonging patients' life expectancy. In contrast, the fundamental goal of gene therapy is to address the underlying genetic cause of these diseases by targeting the specific genetic regions responsible for the disorder.

Adeno-associated virus (AAV) vectors, employed in gene therapy, are chosen based on the target gene, with different serotypes offering varying levels of efficacy. AAV9 vectors, in particular, are considered the most suitable for DMD due to their ability to target a variety of tissues and systems. The low immunogenicity of AAV9, coupled with its favorable size, allows for the delivery of appropriate doses, which can result in minimal tissue damage and maximal therapeutic efficacy.

Beyond vector selection, the method of delivery - how the vector is introduced into the body - plays a critical role. Various injection techniques are employed to enhance therapeutic effects and ensure safe and efficient delivery to target tissues. This research focuses on the long-term effects, safety, and potential of gene transfer therapy using AAV9 vectors in the treatment of Duchenne muscular dystrophy. In the future of neuromuscular medicine, gene therapy utilizing vector-based systems may prove to be even more promising than currently anticipated.

19. ENDOMETRIOTIC LESIONS AND THEIR RECURRENCE: A STUDY ON THE MEDIATORS OF IMMUNOREGULATORY (TGF- β /MIRNA)

Fateme Montazeri, Seyed Mehdi Hoseini, Maryam Abdoli

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Endometriosis is a prevalent estrogen-dependent disorder characterized by ectopic implantation of endometrial tissue, often leading to chronic pelvic pain, infertility, and frequent recurrence post-surgery. Emerging evidence highlights the crucial role of miRNAs and immunoregulatory mediators in the pathogenesis and progression of the disease.

In this study, eutopic and ectopic endometrial tissues from 20 women with confirmed endometriosis and 20 controls were analyzed for the expression levels of miR-20A, miR-145, miR-191-5p, and miR-122-5p, along with their respective target genes, TGF- β and NANOG. Our results demonstrated a significant upregulation of TGF- β and NANOG in endometriotic tissues, accompanied by elevated miR-20A and miR-145 expression. A negative correlation was observed between miR-145 and NANOG expression.

ROC analysis revealed miR-145 as a potential diagnostic biomarker, whereas miR-20A expression correlated with recurrence risk. Moreover, bioinformatics analysis identified miR-191-5p downregulation and miR-

122-5p upregulation in ectopic lesions, with plasma levels notably increased in recurrent cases. Enrichment analysis suggested that these miRNAs regulate pathways involved in tight junction integrity, immune response, mitochondrial metabolism, and epigenetic modifications.

These findings underscore the relevance of miRNA-mediated regulatory networks in endometriosis pathogenesis and recurrence, suggesting that miR-20A, miR-145, miR-191-5p, and miR-122-5p may be promising non-invasive biomarkers and therapeutic targets.

20. NETWORK-BASED INVESTIGATION OF MIRNA AND MICROBIOME INTERACTIONS IN CRC: A SYSTEMS BIOLOGY APPROACH

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Colorectal cancer (CRC) is a complex disease influenced by genetic, epigenetic, and environmental factors, including host-microbiome interactions. miRNAs have emerged as key post-transcriptional regulators in CRC, modulating gene expression and cellular pathways. Additionally, recent studies suggest a critical role of the gut microbiome in CRC progression, with certain bacterial taxa influencing host gene expression. However, the integrated regulatory landscape of miRNA-microbiome-host interactions remains poorly understood. This study aims to construct a directed multi-omics regulatory network integrating miRNAs, transcription factors (TFs), proteins, and microbiome interactions to identify disease-specific functional modules in CRC.

We developed a directed network model incorporating experimentally validated miRNA-TF, TF-protein, and microbiome-gene interactions from multiple databases, including miRTarBase, TargetScan, SIGNOR, and GutMGene. Differentially expressed or repressed genes (DEGs) from GSE41258 were mapped onto the network to extract a CRC-related subgraph. Louvain clustering was applied to identify functional modules within the network. Enrichment analysis was performed to determine biological pathways regulated by miRNA-microbiome interactions in CRC.

The network-based analysis identified key miRNAs and microbial species as potential regulators of inflammatory and oncogenic pathways in CRC. Functional clustering revealed distinct regulatory modules, where miRNAs co-regulate cancer-related genes alongside microbiome-influenced pathways such as immune response, epithelial barrier function, and metabolic dysregulation.

This study provides a systems biology framework to explore host-microbiome-miRNA interactions in CRC, identifying key regulatory nodes that could serve as novel biomarkers or therapeutic targets. Our network-driven approach offers new insights into the molecular crosstalk between the microbiome and host regulatory machinery, paving the way for precision medicine strategies in CRC treatment.

21. GENE THERAPY IN HEMOGLOBINOPATHIES

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Current treatments for hemoglobinopathies consist primarily of disease-modifying therapies that reduce disease severity but do not correct the underlying cause. Allogeneic hematopoietic stem-cell transplantation (HSCT) from an HLA-matched sibling donor is a potentially curative option. However, its use is limited because fewer than 20% of patients have an HLA-matched sibling donor, and there are risks of graft-vs.-host disease (GVHD) as well as complications associated with immunosuppression and graft rejection, which can be fatal.

Exagamglogene autotemcel (exa-cel) is a non-viral, autologous cell therapy designed to reactivate fetal hemoglobin production through *ex vivo* clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 gene editing at the erythroid enhancer region of BCL11A in a patient's own hematopoietic stem and progenitor cells (HSPCs). BCL11A is a transcription factor that represses the expression of fetal hemoglobin in erythroid cells after birth. Elevated levels of fetal hemoglobin are associated with reduced morbidity and mortality in sickle cell disease and β -thalassemia.

22. IDENTIFICATION AND FUNCTIONAL CHARACTERIZATION OF MCPH1/BRIT1 SYNTHETIC LETHAL GENES TO TREAT BREAST CANCER

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The tumor suppressor gene MCPH1/BRIT1 has been shown to play several functional roles in breast cancer (BC), including BC development and inheritance. Reduced MCPH1/BRIT1 expression has been identified in approximately one-third of BC patients, particularly in partially aggressive BC and triple-negative BC.

The objective of this study is to identify potential treatments for these patients using a synthetic lethality (SL) approach targeting MCPH1/BRIT1. To achieve this, SL gene candidates for MCPH1/BRIT1 were identified via two high-throughput siRNA screens performed in U2OS cells, which were transfected with 7,752 genes with and without MCPH1/BRIT1 siRNA knockdown.

BRD4 was prioritized as an SL gene based on six filtering criteria: (1) a $\geq 40\%$ difference in cell viability between the two siRNA screens, (2) gene expression in the U2OS cell line (14.9), (3) normal breast tissue (20.4), (4) the impact of gene expression on BC patient survival, (5) availability of the inhibitor JQ1, and (6) functional similarity with MCPH1/BRIT1, including DNA repair, cell cycle regulation, transcription and telomere regulation, and chromosome condensation.

Next, colony formation assays (CFAs) were performed to determine the optimal BRD4 inhibitor range for BC cell lines MDA-MB-468, MCF7, MDA-MB-231, and T47D. Subsequently, BRD4 inhibitor CFAs were performed on siControl and siMCPH1/BRIT1 knockdown MDA-MB-468 and MCF7 cells. The BRD4 inhibitor caused a greater reduction in cell number in siMCPH1/BRIT1 knockdown cells compared with siControl in both cell lines.

Currently, inhibition of cell proliferation and induction of apoptosis are being investigated to determine the cause of the reduced cell number following siMCPH1/BRIT1 knockdown and BRD4 inhibitor treatment. Additionally, RNA-Seq will be performed on siControl and siMCPH1/BRIT1 knockdown BC cells after

BRD4 inhibitor treatment to elucidate the SL mechanism between MCPH1/BRIT1 and BRD4.

23. APPLICATION OF HUMAN STEM CELL-DERIVED 3D SPHEROIDS AND ORGANOID FOR DRUG DEVELOPMENT

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Human induced pluripotent stem cells (iPSCs) provide an excellent source for generating differentiated tissues, including liver, blood vessel, cardiac, and neural cell types. These tissues can be successfully applied in *in vitro* drug development or toxicology studies, and in many cases, they can replace animal models. Recently, 3D cultures and organoids have become indispensable tools in drug development and evaluation, as various organoids can be obtained *in vitro*, representing most human organs. Unlike 2D cultures, 3D models enable the formation of complex tissue structures, cell-cell communication, and cell-matrix interactions, allowing for the study of intricate biological processes in a broad range of applications, including drug discovery, regenerative medicine, and disease modeling.

While surgically obtained human cells and organoids face significant challenges in availability and reproducibility, iPSC-derived human 3D organoids have the potential to become essential preclinical models for research and drug development. Specific disease models from gene-edited human pluripotent stem cells can be reproducibly generated, and after targeted differentiation, these can serve as preclinical models for screening new drugs for effective treatment.

However, such human models require specific conditions, including a GLP-compliant environment for organoid generation and drug screening. In this regard, important steps must be taken to achieve standards for proper iPSC-derived organoid development, as well as for screening or toxicology studies, satisfying all regulatory requirements in developed countries.

24. THE EFFECT OF EPIGENETICS ON LONGEVITY

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Understanding longevity has become one of the most important research fields in the current century. Longevity investigates how healthy aging can be achieved, including in individuals who are genetically at higher risk for certain diseases, while also focusing on efforts to reverse the detrimental effects of aging and extend lifespan. Understanding the role of genetic, epigenetic, molecular, and environmental regulatory factors in aging, as well as the mechanisms behind different theories of aging, can contribute to the development of appropriate diagnostic, therapeutic, and preventive strategies.

Epigenetic mechanisms regulate various biological and psychological processes through the modulation of gene expression. One of the most conserved hallmarks of aging is epigenetic change, including DNA methylation, histone modifications, chromatin remodeling, non-coding RNAs, and extracellular RNAs. While numerous biological processes and markers contribute to aging, epigenomic changes are particularly

notable due to their central role in gene regulation and cellular identity.

Within the cell nucleus, DNA is wrapped around histone proteins, forming a compact, packaged structure. Throughout human development, exposure to environmental factors such as stress, toxins, and nutrition dynamically influences histone number and structure. One key biochemical process is histone acetylation, which loosens the compacted DNA structure, leading to increased expression of genes in that region. Consequently, the structural or functional proteins, hormones, or enzymes encoded by these genes are synthesized in greater amounts. Conversely, the removal of acetyl groups from histone tails - known as deacetylation - results in reduced gene expression, often referred to as gene silencing, which may lead to lower synthesis of necessary proteins, hormones, or enzymes.

Histones can also undergo other modifications, such as phosphorylation, methylation, and ubiquitination, all of which dynamically influence gene expression. These modifications provide a complex strategy for either enhancing or repressing gene activity.

Another critical epigenetic process is DNA methylation. The addition of a methyl group to cytosines within the DNA sequence represents a more stable and long-lasting epigenetic modification. Methylation generally makes DNA less accessible, leading to gene silencing. This process is essential for producing the diversity of cell types in the body, enabling the formation of differentiated neurons, blood cells, or muscle cells, which are genetically identical but have distinct epigenetic profiles. Thus, a cell's epigenetic characteristics determine its gene expression patterns, defining its phenotype and functional properties.

This study aims to demonstrate the biochemical effects of histone modifications and DNA methylation on epigenetic changes that influence longevity.

25. NON-O BLOOD TYPES ARE ASSOCIATED WITH A GREATER RISK OF LARGE ARTERY ATHEROSCLEROSIS STROKE AND DYSREGULATION OF CHOLESTEROL METABOLISM: AN OBSERVATIONAL STUDY

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Previous research on ABO blood types and stroke risk has been controversial, with non-O blood types generally associated with higher susceptibility. This study investigated the relationship between ABO blood groups and ischemic stroke (IS) subtypes, particularly large artery atherosclerosis (LAA), within a Chinese cohort. We analyzed 9,542 IS patients and inferred their blood types using two ABO gene loci (c.261G>del;

c.802G>A), comparing them to a healthy control group derived from the 1000 Genomes Project. Non-O blood types were significantly more prevalent among stroke patients (70.46%) compared to healthy individuals (61.54%), with LAA being the most frequent subtype in non-O blood type patients. Clinical baseline characteristics, including low-density lipoprotein cholesterol (LDL-C) levels, activated partial thromboplastin time, and thrombin time, showed significant variations among blood types, suggesting potential biological differences. Further analysis using volcano plots revealed 17 upregulated and 42 downregulated proteins in O blood type individuals. Gene ontology (GO) analysis indicated that the downregulated proteins were primarily involved in lipid metabolism pathways. To further explore this mechanism, *in vitro* experiments were conducted using HT29 and SW480 cell lines with reduced ABO gene expression. The results demonstrated that decreased ABO expression led to reduced cholesterol uptake and increased cholesterol efflux, implicating a role for ABO blood groups in cholesterol regulation. These findings suggest that non-O blood types may increase the risk of LAA stroke through disruptions in cholesterol metabolism. This study provides novel insights into the mechanisms linking ABO blood types to stroke subtypes and highlights the importance of lipid metabolism pathways in stroke pathogenesis.

26. ASSOCIATION BETWEEN GENETIC FACTORS AND THE EFFECTIVENESS OF PLATELET-RICH PLASMA IN THE TREATMENT OF TENNIS ELBOW

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Platelet-rich plasma (PRP) therapy is commonly used in the treatment of various types of injuries, such as Achilles tendinopathy, knee osteoarthritis, or tennis elbow. PRP contains a high concentration of growth factors that are responsible for its therapeutic properties. However, its effectiveness remains debatable. According to our hypothesis, individual differences in PRP efficacy may be influenced by genetic variation. Our research has shown that single nucleotide polymorphisms (SNPs) in genes encoding growth factors and their receptors are associated with treatment outcomes. Studied genes included platelet-derived growth factor alpha (PDGFA), platelet-derived growth factor beta (PDGFB), vascular endothelial growth factor A and B (VEGFA, VEGFB), transforming growth factor beta 1 (TGFB1), platelet-derived growth factor receptor alpha (PDGFR- α), and platelet-derived growth factor receptor beta (PDGFR- β). Furthermore, polymorphisms in the COL1A1 gene have been shown to be associated with pain perception. The effectiveness of therapy was assessed using patient-reported outcome measures (PROMs), specifically the visual analog scale (VAS), the quick version of the disabilities of the arm, shoulder, and hand (QDASH), and the patient-rated tennis elbow evaluation (PRTEE). Treatment efficacy was analyzed at multiple follow-up points after PRP injection (weeks 2, 4, 8, 12, 24, 52, and 104). Differences between baseline and follow-up results were calculated for all PROMs (Δ VAS, Δ QDASH, and Δ PRTEE) and compared across the respective genetic variants. Our results suggest that genetic factors may influence the efficacy of PRP therapy. Genotyping specific polymorphisms of the studied genes may help in selecting patients most likely to benefit from PRP therapy. Choosing the right treatment strategy for each patient could lead to faster and more cost-effective health improvements.

27. EPIGENETIC REPROGRAMMING BY MESENCHYMAL STEM CELLS AND EXOSOMES: A NOVEL THERAPEUTIC STRATEGY FOR AUTOIMMUNE DISEASES

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Autoimmune diseases arise from dysregulated immune responses, often driven by epigenetic aberrations that alter gene expression and immune cell function. Mesenchymal stem cells (MSCs) and their exosomes (MSC-EXO) offer a groundbreaking therapeutic approach by modulating epigenetic landscapes, restoring immune tolerance, and suppressing chronic inflammation. This study explores the mechanisms by which MSCs and MSC-EXO regulate DNA methylation, histone modifications, and non-coding RNA pathways to reverse autoimmune pathology.

MSC-mediated DNA methylation plays a pivotal role in immune regulation. By upregulating DNA methyltransferases (DNMT1, DNMT3A), MSCs reinforce promoter methylation of inflammatory genes, thereby dampening excessive immune activation. In inflammatory bowel disease (IBD), MSCs and MSC-EXO enhance METTL3/IGF2BP3-mediated m6A RNA modifications, stabilizing pre-miR-34a and increasing miR-34a-5p expression, which promotes intestinal epithelial repair. In systemic lupus erythematosus (SLE), MSCs counteract global hypomethylation in CD4⁺ T cells by downregulating miR-148a and miR-21, preventing DNMT1 suppression and re-establishing regulatory T cell (Treg) function through FOXP3 induction via TGF- β 1 signaling.

Histone modifications further reinforce MSC-mediated immunomodulation. MSC-EXO enhances histone deacetylase (HDAC) activity, leading to hypoacetylation of NF- κ B target genes and suppression of pro-inflammatory cytokine expression. Additionally, MSCs regulate histone methylation, particularly H3K27me3 enrichment at pro-inflammatory gene loci, silencing their transcription. In macrophages, MSC-EXO promotes the transition from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype by modifying chromatin accessibility and increasing IL-10 and arginase-1 expression via H3K4me3 methylation.

These findings position MSCs and MSC-EXO at the forefront of next-generation regenerative medicine for autoimmune diseases. By leveraging their epigenetic reprogramming capabilities, MSC-based therapies offer a paradigm shift in precision medicine, paving the way for innovative, long-term solutions to immune dysregulation.

28. THE IMPORTANCE OF NUTRIGENETIC TESTING IN DETOXIFICATION

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The purpose of this study was to evaluate the effectiveness of non-invasive simultaneous electrical stimulation of the vagus and trigeminal nerves in patients with migraine, using both a visual analog scale (VAS) and EEG signal analysis recorded from the left prefrontal lobe during concentration tasks.

The methods involved designing and constructing an instrument capable of stimulating both nerves simultaneously. Stimulation parameters were set at 60 Hz, 4 mA, and 0.2-0.3 ms pulse duration for the trigeminal nerve, and 1 Hz, 2 mA, and 0.2-0.3 ms for the vagus nerve. Twelve 30-min sessions were administered three times per week over a one-month period.

Frontal lobe EEG activity was recorded using a TGAM-sensor-equipped headband while participants played an electric buzz wire game, both before and after the 12-session treatment period. Pain intensity and seizure frequency were also assessed before and after treatment.

The main findings indicate that the intervention led to reductions in both seizure frequency and pain intensity. Post-treatment EEG analysis revealed potential changes in brain activity, with notable alterations observed in Beta and Low Alpha oscillations.

29. NUCLEAR PHOSPHATIDYLSERINE (PS) ACTIVELY REGULATES THE CELLULAR LIPID METABOLISM AND THE NUCLEAR ENVELOPE DEFORMATION

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Phosphatidylserine (PS) is a major anionic phospholipid essential for various biological processes, including cell signaling, apoptosis, and immune responses. In mammalian cells, PS is synthesized by the phosphatidylserine synthase enzymes PSS1 and PSS2. The activity of both enzymes is inhibited by their product, PS, a phenomenon known as product PS-mediated feedback inhibition. Mutations in PSS1 that confer resistance to this feedback inhibition lead to excessive PS production, which is a causative factor in the rare disease Lenz-Majewski syndrome (LMS). Given the critical role of PS in physiological processes and in LMS patients, extensive research has been conducted to elucidate its distribution and function across various cytoplasmic compartments. Surprisingly, however, the presence and function of PS in the nucleus have remained unexplored. To address this gap, we developed nuclear-targeting PS biosensors and, for the first time, successfully visualized PS enrichment within the inner nuclear membrane (INM) and the associated nucleoplasmic reticulum (NR). Subsequently, we manipulated PS levels using either PSS1 mutants associated with LMS to elevate PS or nuclear-targeting phosphatidylserine decarboxylase (PSD1) to reduce PS within the INM and NR, allowing us to elucidate its function. This approach revealed that PS enrichment within the INM and NR is required for the recruitment of CCT α and Lipin1 α - two essential rate-limiting enzymes for phosphatidylcholine (PC) biosynthesis - from the nucleoplasm to the INM and NR in response to oleic acid overload. Furthermore, we demonstrated that PS availability directs the lipid metabolic flux toward PC synthesis for membrane expansion rather than lipid storage. These results uncover a previously unrecognized regulatory role of PS enrichment in the INM and NR in modulating phospholipid flux through the membrane translocation of two key PC-synthesizing enzymes. Additionally, we generated cell lines with inducible expression of nuclear PS biosensors to track dynamic changes of PS within the INM and NR in the context of nuclear envelope deformation, which has been linked to various human diseases, including tumorigenesis. Several nuclear downstream effectors of PS associated with this process have been identified, and ongoing studies aim to further explore their roles. These findings provide significant insights into the dynamic regulation of PS within the INM and NR and its broader impact on cellular processes.

30. RS12826786 LNCRNA HOTAIR POLYMORPHISM IN PATIENTS WITH ULCERATIVE COLITIS: AN EXPERIMENTAL STUDY

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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by abnormal immune responses that cause inflammation and ulcers in the inner lining of the large intestine. Chronic inflammatory bowel diseases are associated with persistent activation of signaling pathways, including nuclear transcription factor kappa B (NF- κ B), cyclooxygenase, and interleukins. The long non-coding RNA (lncRNA) *HOTAIR* contains binding sites for multiple transcription factors, including activator protein, specificity protein, estrogen responsive element, hypoxia-responsive element, and NF- κ B.

Methods: In this study, fifty individuals with UC and sixty healthy, age- and sex-matched controls were recruited. Genotyping of *rs12826786* in the *HOTAIR* gene was performed using tetra-primer amplification refractory mutation system PCR (T-ARMS PCR). Additionally, *HOTAIR* gene expression was quantified using real-time PCR.

Results: The study investigated the association between *HOTAIR* genotypes and UC. The frequencies of TT, CT, and CC genotypes in UC patients were 30%, 26%, and 44%, respectively, compared to 10%, 40%, and 50% in controls. Statistical analysis revealed a significant correlation between the *HOTAIR* gene polymorphism and UC. Odds ratio analysis indicated that individuals with the TT genotype had a threefold higher risk of developing UC. Gene expression analysis showed higher *HOTAIR* expression in UC patients compared to controls, with the TT genotype exhibiting the highest expression levels.

Conclusion: This study highlights the potential role of lncRNA *HOTAIR* in UC pathogenesis and underscores the significance of the *rs12826786* polymorphic locus in modulating disease susceptibility.

31. REVOLUTIONIZING OPHTHALMOLOGY WITH DEEP LEARNING: AUTOMATED RETINAL IMAGE CLASSIFICATION FOR DISEASE DIAGNOSIS

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Eye diseases, including diabetic retinopathy, cataracts, and glaucoma, are leading causes of vision impairment worldwide, affecting an estimated 2.2 billion individuals. Early detection and timely intervention are critical to preventing irreversible blindness. DeepSight presents a robust Convolutional Neural Network (CNN)-based model designed to classify retinal images into four categories: normal, diabetic retinopathy, cataract, and glaucoma. The study utilized a dataset of 4,217 high-resolution retinal images sourced from databases such as IDRiD, Ocular Recognition, and HRF, with balanced representation across all classes. Preprocessing techniques were applied to enhance image features, ensuring high-fidelity input for classification. The CNN architecture integrates advanced convolutional layers for spatial feature extraction and dense layers for precise classification. The model was trained using categorical cross-entropy loss and optimized with the Adam optimizer, achieving an overall accuracy of 92.3%, with precision, recall, and F1-scores exceeding 90% across all categories. These results demonstrate the model's ability to reliably distinguish between healthy and diseased eyes. DeepSight's platform not only automates the diagnostic process but also addresses critical gaps in healthcare accessibility, particularly in resource-limited settings. By providing real-time, AI-powered diagnostic support, it empowers ophthalmologists with actionable insights and patients with timely detection of eye conditions. Future integration into clinical workflows aims to enhance diagnostic efficiency, improving patient outcomes. This research underscores the

transformative potential of artificial intelligence in ophthalmology, establishing a benchmark for AI-driven diagnostic tools in medical imaging.

32. EVALUATING THE ACCURACY OF MULTIPLE RAPID DIAGNOSTIC TESTS FOR HIV DETECTION IN SERUM SAMPLES ANALYSED DURING POINT-OF-CARE PROFICIENCY TESTING ASSESSMENTS

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Background: HIV rapid diagnostic tests (RDTs) are essential for timely diagnosis and early initiation of treatment, particularly in resource-limited settings. The World Health Organization recommends that HIV RDTs achieve a minimum sensitivity of $\geq 99\%$ and specificity of $\geq 98\%$ to ensure diagnostic accuracy. This study aimed to evaluate the performance of HIV RDTs through a proficiency testing program, with the goal of identifying regional disparities and areas needing improvement across nine provinces in South Africa.

Methods: This cross-sectional study was conducted from April to June 2023 by the National Health Laboratory Service. A total of 25,458 blinded serum samples, including both HIV-positive and HIV-negative specimens, were distributed to testing facilities across all nine provinces. HIV RDTs were used for both screening and confirmatory testing, and results were submitted via a centralized portal. Key performance metrics - sensitivity, specificity, positive predictive value, and negative predictive value - were calculated. Concordance between test results was assessed using Cohen's Kappa statistic.

Results: The study achieved a 98.25% response rate, with overall sensitivity and specificity of 98.7% each. The overall agreement was 98.7% ($\kappa = 0.97$, $P < 0.001$). However, significant regional differences were observed. The Northern Cape showed higher rates of false negatives and false positives, with sensitivity and specificity as low as 91.8% and 92.0%, respectively. In contrast, Gauteng, KwaZulu-Natal, and Mpumalanga performed exceptionally well, with both sensitivity and specificity exceeding 99%.

Conclusion: While HIV RDTs generally performed well nationwide, certain regions - particularly the Northern Cape - require targeted interventions to improve test accuracy. Regular proficiency testing, enhanced training, and continuous quality assurance are recommended to ensure reliable HIV diagnostics across South Africa.

33. GENE-MEDIATED EFFECT OF BACILLUS SUBTILIS ON ENHANCEMENT OF THE PH OF ACIDIC FOOD ITEMS

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Previous studies have shown that *Bacillus subtilis*, a probiotic, can withstand gradual changes in both acidic and basic conditions. It recovers growth more rapidly when the pH shift is from high to low, compared to shifts from low to high pH, likely due to greater genetic adaptations required in the latter case. In acidic

environments, bacterial genes such as *adhA* and *psd* are upregulated, promoting the production of dehydrogenases and decarboxylases, respectively. These enzymes are primarily responsible for consuming acids. Most earlier studies focused on the regulatory effects of *Bacillus subtilis* on large-scale industrial wastes containing acidic and basic compounds. In this study, we investigated the effect of the bacterial culture on acidic food items and preservatives encountered in daily life. Upon addition of the non-pathogenic bacteria to various items - such as lemon and tomato juices, as well as vinegar - there was a significant increase in pH compared to the original samples. The greatest pH shift was observed in tomato juice, followed by lemon juice and vinegar. This small-scale study supports the concept that *Bacillus subtilis* activates acid-consuming genes in acidic environments, leading to increased pH. However, larger and more comprehensive studies are needed to confirm the acid-neutralizing effect of *Bacillus subtilis* before it can be recommended as a dietary supplement, particularly for individuals suffering from gastroesophageal reflux disease (GERD), commonly known as acid reflux.

34. GERD: LATEST UPDATE ON ACID-SUPPRESSANT DRUGS

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GERD is a well-known diagnosis among healthcare providers due to its widespread prevalence, and its symptoms can significantly impact the quality of life for a substantial proportion of patients. Consequently, the ongoing pursuit of treatments that not only relieve symptoms but also minimize side effects remains a logical and necessary goal, given the large demographic affected by GERD. In this review, we analyze GERD, including the potential regulatory effects of certain drugs on the pathways implicated in the disease.

35. THE MONOGENIC FORMS OF OBESITY IN SAUDI FAMILIES

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Background: Obesity is a complex biological and hereditary disorder. Most monogenic changes causing obesity have been identified in samples from related families and diverse populations. In the present study, we aimed to explore the “missing heritability” of obesity by focusing on extreme phenotypes, which are likely enriched for rare variants. This approach improves the power to identify loci that may reveal novel or rare variants. We specifically targeted extreme subgroups of obese patients to identify known and novel loci in the Saudi Arabian population.

Aims: To investigate the genetic contribution to obesity in Saudi Arabia and identify monogenic mutations responsible for obesity in adults (BMI ≥ 30 kg/m²) and children (BMI above the 90th and 97th percentiles, respectively) within consanguineous families.

Methods: Samples were collected from eight Saudi families, each comprising nine individuals with a range of BMI from healthy to obese. Whole-Exome Sequencing (WES) was employed to screen for known and potentially novel obesity genes in multiplex consanguineous families. Variants were filtered manually from VCF files and analyzed using the AI-based software Diploid (Moon). Candidate genes identified through this approach were validated using Sanger Sequencing.

Results: Manual filtration identified 14 candidate genes, of which PCR validation for seven genes was negative. The AI analysis via Diploid (Moon) generated a comprehensive list of rare variants and candidate obesity genes. Across all families, 35 rare genes with 40 variants were identified, with 19 candidate genes harboring 28 variants. Overall, results highlighted both novel and previously described mutations associated with extreme obesity phenotypes.

Conclusion: Our study confirms that both homozygous and heterozygous mutations occur in candidate obesity genes in these families. Affected individuals exhibited extreme obesity, supporting the polygenic nature of obesity and its strong interaction with environmental factors.

36. TUMOR RECOGNITION FROM MEDICAL IMAGES USING CONVENTIONAL AND DEEP-LEARNING TECHNIQUES

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Cancer remains a severe and widespread disease, with abdominal tumors such as liver and pancreatic cancers, as well as brain tumors, among the most frequent and deadly forms. While biopsy is currently the gold standard for diagnosis, it is invasive and carries risks including infection and tumor dissemination. Non-invasive, image-based computer vision methods provide a promising alternative for accurate and automatic tumor detection. In this study, both conventional and deep learning approaches, as well as their combinations, were applied to ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) for tumor recognition. Deep learning models, including standard and enhanced Convolutional Neural Networks (CNNs) such as ResNet101, InceptionV3, EfficientNet_b0, and EfficientNet_b0 with Atrous Spatial Pyramid Pooling (ASPP), were evaluated at classifier and decision levels for liver and pancreatic tumors in US and CT images, and for brain tumors in MRI images. Additionally, domain adaptation learning was employed, training CNNs on multi-tumor datasets and fine-tuning them for specific tumor types, to improve classification performance. The results showed that deep learning methods consistently outperformed conventional techniques, achieving maximum accuracies exceeding 96% for liver tumors and above 99% for pancreatic and brain tumors. These findings demonstrate the potential of advanced deep learning architectures and domain adaptation strategies as reliable, non-invasive tools for computer-aided cancer diagnosis across multiple imaging modalities.

DECLARATIONS

Authors' contributions

The author contributed solely to the article.

Availability of data and materials

They can contact the corresponding author to request the data and receive a response.

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Not applicable.

Consent for publication

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