SOFIA UNIVERSITY
St. KLIMENT OHRIDSKI

ACADEMIA-INDUSTRY PARTNERING SYMPOSIUM "BIOMARKERS IN TRANSLATIONAL MEDICINE"

28 November 2025
Grand Hotel Sofia

BOOK OF ABSTRACTS
FROM POSTER SESSION

НАЦИОНАЛНА ПЪТНА КАРТА
ЗА НАУЧНА ИНФРАСТРУКТУРА
(2020-2027 г.)
МИНИСТЕРСТВО НА ОБРАЗОВАНИЕТО И НАУКАТА
РЕПУБЛИКА БЪЛГАРИЯ
▸ 2020

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И НАУКАТА

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Sofia 2025

EATRIS-Bulgaria Organizing Committee:

Prof. Rossitza Konakchieva - National Director
Assoc. Prof. Georgi Nikolaev - National Coordinator
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Ministry of Education and Science of Bulgaria under Grant &DO1-361/2023 and H2020 Project EATRIS-Connect

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28 November 2025
Grand Hotel Sofia, Sofia

PROGRAM

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Opening and Welcome addresses
Ministry of Education and Science- Science Directorate
SU "St. Kliment Ohridski"-**Acad. Tony Spassov, Vice-Rector**
Faculty of Biology – **Assoc Prof. Luben Zagortchev**, Dean
Introduction to 2025 EATRIS-Bulgaria Georgi Nikolaev, NC

10:30 – 13:00 SESSION "AI AND DIGITALIZATION OF TRANSLATIONAL MEDICINE"
10:30 – 10:50 - EATRIS Digital Hub –
Nektarios Liaskos, EATRIS, Data Strategy Manger,
EATRIS C&S office
10:50 – 11:10 - Health Industry and Academic Research partnership to foster innovation in precision medicine, Health & Life Science Cluster Bulgaria
Kristina Eskenazi, Chairwoman of HLSB
11:10 – 11:30 - Data Governance, Data Stewardship, Cybersecurity - Digital Innovation Hub "TRAKIA" Cyber4All,
Hristyan Daskalov, Chairman of EDIH
11:30 – 11:50 - Bridging the gap to precision medicine:
Bulgarian Hub for genomic data, part of European Genomic data infrastructure (GDI) and Genome of Europe Project
Radka Kaneva, BBMRI-BG Coordinator, Exec Manager of MMC, MU-Sofia

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12.00 – 12.40 Discussion panel: "European Digital Health Data Spaces and AI Factories for Biomarker Innovation"
Moderator:
Kristina Eskenazi, HLSB
Participants:
Irena Pavlova, Manager EU Projects, GATE Institute,
Simeon Stoyanov, Business Manager
(Brain ++/Petascale Discoverer), Member of EuroHPC
Georgi Kaludov, IBM Accelerator Bulgaria
- European Digital Health Data Spaces (VELES project case study)
- AI Factory serving innovations in Biomarker Research

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PROGRAM

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Ritika Kulshreshtha, SINGLERON Biotechnologies, Germany

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Soren Hayrabedyan, IBIR "Acad. K. Bratanov"- BAS

15.20 – 15.40 - Ikaros Deletions among Bulgarian Patients with Acute Lymphoblastic Leukemia/Lymphoma
Stephan Lozenov, SU "St. Kliment Ohridski"

15.40 – 16:00 - HMGB1 as a Biomarker and Therapeutic Target in Triple-Negative Breast Cancer: Inhibitory Effects of Metformin on HMGB1/RAGE Signaling
Shazie Myashkova, IMB "Roumen Tsanev" – BAS

16:00 – 16.20 Implementation of AI in medically assisted reproduction (MAR)
Georgui Nikolov, Director, ReproBioMed

16.20 – 16:30 General discussion

16:30 – 17:00 – Coffee break, Online Poster session

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PROGRAM

Junior Award Session

17:00–17:10 Integrated Transcriptomics analysis reveals key drivers of aggressiveness in Pancreatic adenocarcinoma (PAAD)
Krasimira Russinova-Ilieva, Molecular Medicine Center, Department of Medical Chemistry and Biochemistry, Medical Faculty, Medical University of Sofia

17:10–17:20 Distribution of Wild-Type Optineurin and Mutant p.Glu135Ter in MDCK-II Cells
Jong Hun Park, Faculty of Biology, Sofia University "St. Kliment Ohridski"

17:20–17:30 Long COVID - related endothelial injury: Evidence of ORF3a-induced mitochondrial dysfunction in SARS-CoV-2-infected endothelial cells
Yuliia Mariienko, Laboratory of Reproductive OMICs Technologies, Institute of Biology and Immunology of Reproduction – BAS

17:30-17:40 Effect of mesenchymal stem cells on the proliferation and estradiol secretion of human granulosa cells under hypoxic and inflammatory conditions
Kalina Belemezova, Department of Biology, Medical Faculty, Medical University - Sofia

17:40-17.50 VASA (DDX4) and DAZL - positive Differentiation of Primordial Germ Cell-like Cells from hESCs Using BMP-4 and hAFSC-4 Conditioned Medium
Borislav Arabadzhijev, Faculty of Biology, Sofia University "St. Kliment Ohridski"

17:50 – 18:00 – Closing conference sessions

ABSTRACTS
FROM POSTER SESSION

HMGB1 as a Biomarker and Therapeutic Target in Triple-Negative Breast Cancer: Inhibitory Effects of Metformin on HMGB1/RAGE Signaling

SHAZIE YUSEIN-MYASHKOVA[1*], DESISLAVA VLADIMIROVA[1],
MIHAELA ALEKSANDROVA[2], IVA UGRINOVA[1], JORDANA TODOROVA[1]

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Key words: EMT (epithelial-mesenchymal transition), HMGB1, RAGE, Breast cancer, metformin

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High-mobility group box 1 (HMGB1) is a nuclear protein that is overexpressed in various cancers, including triple-negative breast cancer (TNBC), where it promotes tumor progression through interaction with the receptor for advanced glycation end products (RAGE). Metformin, a widely used antidiabetic drug, has gained attention for its anticancer properties. Notably, metformin can directly bind to HMGB1 and inhibit its pro-inflammatory functions, making it a promising candidate for targeting HMGB1/RAGE signaling.

This study investigates the effects of metformin on HMGB1/RAGE signaling in TNBC cells. Metformin significantly inhibits HMGB1-induced cell migration, as shown by wound-healing assays. Immunoblotting and immunofluorescence analyses reveal that metformin reduces HMGB1 and RAGE expression, disrupts NF-κB signaling, and reverses epithelial-to-mesenchymal transition by increasing E-cadherin and decreasing vimentin. These findings suggest that tumors with high HMGB1 and RAGE expression may be particularly responsive to metformin treatment, supporting the potential for biomarker-guided therapeutic strategies in TNBC.

Acknowledgement: This project is funded by Bulgarian National Scientific Fund, project №: КП-06-Н51/13

Integrated Transcriptomics analysis reveals key drivers of aggressiveness in Pancreatic adenocarcinoma (PAAD)

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Keywords: Transcriptomics, Pancreatic cancer, Biomarkers, Solid tumors

Objective: Pancreatic adenocarcinoma (PAAD) is one of the most lethal solid tumors, characterized by rapid progression, therapeutic resistance, and poor prognosis. The aim of this study was to identify molecular drivers of PAAD aggressiveness through an integrated transcriptomic approach using TCGA data.

Methods: Differential gene expression was analyzed to detect significantly altered genes, followed by pathway and network analyses to identify affected molecular modules and oncogenic mechanisms. Principal component analysis (PCA) was performed to distinguish normal, primary, and metastatic tissues. Survival analyses, including Kaplan–Meier and multivariate Cox regression, were applied to evaluate the prognostic value of candidate genes. Gene–pathway interactions were visualized using network analysis.

Results: Differential expression analysis revealed a set of key upregulated oncogenes and downregulated tumor suppressors. PCA clearly separated tumor from normal samples and revealed a distinct metastatic signature. Survival analyses identified KRAS and TP53 as independent prognostic markers, with KRAS having the strongest impact on overall survival. Network visualization highlighted interconnected oncogenic pathways, suggesting shared mechanisms with other solid tumors.

Conclusion: The transcriptomic analysis identified KRAS and TP53 as major molecular drivers of PAAD aggressiveness and poor prognosis. These findings provide a comprehensive overview of the gene expression alterations in PAAD and highlight potential biomarkers for improved risk stratification and novel therapeutic targets. Future steps will aim to integrate transcriptomic profiling with clinical outcomes, advancing the development of precision oncology in PAAD.

ACKNOWLEDGMENTS: The authors would like to thank Project 3.1.13 “Multi-Omics Approach for Molecular Profiling of Solid Tumors” and the scientific group “Oncogenetics and Genomics”, Medical University – Sofia.

Distribution of Wild-Type Optineurin and Mutant p.Glu135Ter in MDCK-II Cells

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Keywords: optineurin, mutant, ophthalmology, model cell line, transfection

Optineurin (OPTN) regulates vesicular transport, autophagy, and intracellular trafficking. The heterozygous mutation c.403G>T (p.Glu135Ter) causes a premature stop at residue 135, leading to an N-terminal fragment lacking C-terminal domains. This mutation was found in a patient with retinitis pigmentosa, macular degeneration, and myopia. We compared subcellular localization of wild-type and p.Glu135Ter OPTN in polarized MDCK-II epithelial cells, a tractable model with robust polarity and tight junctions relevant to retinal epithelium.

Plasmids encoding wild-type or p.Glu135Ter OPTN were prepared from E. coli XL1-Blue. Endogenous OPTN was confirmed by Western blot. Stable wild-type lines were generated by Escort III transfection, FACS, and single-clone isolation; mutant OPTN was transiently expressed. Localization was assessed by immunofluorescence with co-staining for F-actin, ZO-1, and GM130.

Wild-type OPTN localized predominantly to a perinuclear Golgi-consistent compartment with GM130 colocalization and cytosolic signal. In contrast, p.Glu135Ter formed discrete cytoplasmic clusters and accumulated near the plasma membrane, with increased peripheral colocalization with ZO-1. Both wild-type and mutant signals overlapped with F-actin. Neither construct altered the distributions of F-actin or ZO-1, indicating preserved tight junction organization. Because wild-type was stably expressed and the mutant transient, expression level or stress differences may contribute and should be considered.

The truncated p.Glu135Ter protein exhibits aberrant localization relative to wild-type, with peripheral accumulation and cytoplasmic clustering consistent with altered trafficking and engagement of quality-control or clearance pathways. These data define a cellular defect in OPTN localization and motivate future work to test effects on autophagy flux and vesicular transport dynamics, assess aggregation or clearance pathways, and validate findings in retinally relevant models.

ACKNOWLEDGMENTS

This project was funded by Ministry of Education and Science under contract DO1-178/2022, and the Scientific Research Fund at the Ministry of Education and Science under contract KP-06-N83/7 dated 05.12.2024 and contract 80-10-36 dated 23.05.2025 from the Research Fund of Sofia University, and contract KP-06-N83/7 dated 05.12.2024 from the Bulgarian National Science Fund at the Ministry of Education and Science.

Clearance of Indocyanine green as a new approach to liver function assessment in metabolic syndrome

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Keywords: indocyanine green, clearance, metabolic syndrome, liver function

Objective

This study aims to evaluate the clearance of indocyanine green (ICG), a fluorescent dye completely excreted by the liver, as a marker for assessing liver function in rats with metabolic syndrome (MetS). MetS is an increasingly prevalent global health issue associated with an elevated risk of cardiovascular disease and type 2 diabetes. Liver function is most often affected as a result of the worsening glucose and lipid profile. The assessment of liver function includes measurement of the enzymatic activity of key liver enzymes, which are indicators of liver tissue damage. In this study, simultaneously with the standard protocol, the clearance of ICG was determined as a new approach to liver function assessment. MetS was induced in Wistar rats by a high-fructose diet for 12 weeks. Animals were divided into two groups: with untreated MetS and treated with resveratrol as a dietary supplement. Body weight, blood pressure, blood glucose, triglycerides, and cholesterol levels were monitored weekly. Daily intake of food and fructose solution was recorded. At the end of the experiment, animals were injected with ICG 30 μg/kg b.w. in the tail vein, and blood samples were collected at 5, 10, 15, 30, 45, 60 min, etc. until complete disappearance of the fluorescent signal. Terminal biochemical analyses include detailed lipid profile (HDL, LDL, cholesterol, triglycerides), liver enzymes activity (ALAT, ASAT), and bilirubin plasma level. In the resveratrol-treated (RSV) group, terminal evaluations indicated preserved liver function with lower ASAT activity and decreased bilirubin plasma level compared with the untreated group, but the results are not statistically significant. The same trend of preserved liver function was observed in the ICG clearance assay. In the RSV group a 10-fold lower concentration of the dye was measured in the blood sample at 15th min, and in some animals, there was no fluorescent signal after 60 minutes. Whereas in the untreated group, the signal was noticed even 120 minutes after ICG application. In conclusion, further studies are needed to verify this new approach to evaluate liver function. The method is a promising alternative to the established practice. It allows direct estimation of the preserved working liver capacity, rather than indirectly by the degree of liver tissue damage and accumulated bilirubin. These indicators may be symptoms of other diseases, and not be due to liver damage, such as increased hemolysis or muscle tissue damage.

ACKNOWLEDGMENTS

This research was funded by the Ministry of Education and Science of Bulgaria, Grant DO1-361/2023 "INFRAACT" of NRRI 2020–2027.

Effect of mesenchymal stem cells on the proliferation and estradiol secretion of human granulosa cells under hypoxic and inflammatory conditions

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Keywords: mesenchymal stem cells, granulosa cells, hypoxia, inflammation

Objective:
Premature ovarian insufficiency (POI) is defined as the loss of normal ovarian function before the age of 40. The condition leads to reduced estrogen production, irregular or absent menstrual cycles, and frequently, infertility. Its causes may include genetic factors, autoimmune diseases and exposure to chemotherapy. However, in many cases the disorder is idiopathic, with no identifiable underlying cause. Regardless of their nature, many of these causes are related to the occurrence of a local inflammatory reaction or impaired blood flow, which in turn leads to a lack of nutrients and hypoxia in the ovaries. Granulosa cells (GC) play a pivotal role in the ovarian microenvironment, as they provide both structural and paracrine support necessary for follicular growth, oocyte maturation, and steroidogenesis. Numerous studies have shown the therapeutic effect of MSCs in the treatment of POI through their paracrine effects. The objective was to investigate the effect of MSCs on human granulosa cell proliferation and estradiol secretion under hypoxic and inflammatory conditions.

Methods:
For the purpose of our study, three different experimental setups were set: classical co-cultivation of MSCs and granulosa cells; transwell co-cultivation system, in which the two types of cells do not have direct contact; cultivation of granulosa cells in the presence of conditioned medium obtained from MSCs.

Results:
Overall, our results demonstrated that MSCs suppress GC proliferation under both hypoxic and inflammatory conditions. In contrast, the effects of MSCs on estradiol secretion by GC were variable and dependent on the experimental setup. Direct co-culture of MSCs with GC resulted in increased estradiol secretion under both conditions, a tendency that was similarly observed when conditioned medium from MSCs was applied. However, when MSCs were cultured using transwell inserts, their influence on estradiol secretion was inconsistent, leading to either enhancement or suppression depending on the specific culture conditions.

Conclusion:
The data suggest that MSCs have regulatory effects on granulosa cell function and proliferation in the context of hypoxic and inflammatory conditions. Although further research is needed to standardize MSC production and assess their long-term safety and efficacy, MSCs are undoubtedly an innovative approach, providing an individualized and minimally invasive treatment for reproductive disorders.

ACKNOWLEDGMENTS: The project was funded by the National Research Fund, grant No. КП-06-Н51/2.

Adipokine profiling and mtDNA epigenetic changes in adipose-derived MSCs following palmitic acid treatment

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Keywords: AdMSCs, preadipocytes, mtDNA, adipokines, epigenetic modifications

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Objective: Palmitic acid (PA), a prominent saturated fatty acid found in the diet, is known to induce mitochondrial dysfunction and oxidative stress within metabolic tissues. This study aimed to compare the adipokine secretion patterns between two distinct cell types found in the adipose tissue and known to have different immunomodulatory properties. Additionally, we investigated whether PA influences epigenetic modifications in mitochondrial DNA (mtDNA), utilizing long-read sequencing techniques in adipose-derived mesenchymal stem cells (AdMSCs).

Methods: AdMSCs and preadipocytes were exposed to various concentrations of sodium palmitate for up to 24 h. Secreted adipokines were quantified by LEGENDplex. Total DNA was sequenced on an Oxford Nanopore platform with modified-base calling (6mA) and aligned to the mitochondrial genome.

Results: The adipokine profiles of AdMSCs and preadipocytes exhibited notable differences following brief exposure to PA. Long-read sequencing analysis revelead difference in adenine methylation (6mA), specifically increased hypomethylation after 24 h of palmitate treatment in AdMSCs.

Conclusion: These findings suggest that PA not only alters adipokine secretion but also impacts mitochondrial epigenetic landscape of AdMSCs. These findings motivate single-molecule, heteroplasmy-aware epigenetic profiling as a sensitive readout of lipotoxic stress in metabolic cell models.

ACKNOWLEDGMENTS

Supported by the Bulgarian Ministry of Education and Science Project “Research Infrastructure for Cell Technologies in Biomedicine” (INFRAACT, Grants 178/2022, 361/2023) of the National Roadmap for RI, National Center of Biomedical Photonics (NCBMP DO1- 352), and BG-RRP-2.004-0003 “Research University: Medical University – Pleven”.

Long COVID - related endothelial injury: Evidence of ORF3a-induced mitochondrial dysfunction in SARS-CoV-2-infected endothelial cells

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Keywords: ORF3a, endothelial cells, mitochondrial dysfunction, ROS, Long COVID

Objective

This study investigated how SARS-CoV-2 ORF3a expression affects mitochondrial function in human endothelial cells, aiming to reveal mechanisms underlying endothelial dysfunction and vascular complications associated with post-COVID conditions.

Methods

Human endothelial HULEC-5a cells were cultured and transfected with 0.1 μg/mL ORF3a plasmid DNA. Mitochondrial morphology and structural integrity were assessed label-free using Nanolive 3D holotomography. Cellular oxidative metabolism was evaluated by analyzing reactive oxygen species after incubation with a redox-sensitive dye using Andor confocal microscopy. To quantify oxidative stress, cells were stained with a ROS-specific fluorescent dye, and signal intensity was measured with CellProfiler following confocal imaging.

Results

ORF3a expression induced evident mitochondrial fragmentation and loss of structural integrity, accompanied by a significant increase in ROS fluorescence intensity compared to control cells as ROS were colocalized with ORF3a expression. These findings indicate that ORF3a-expressing endothelial cells undergo oxidative stress.

Conclusion

Our data demonstrate that SARS-CoV-2 ORF3a expression directly disrupts mitochondrial homeostasis. This mechanism may contribute to persistent vascular inflammation, microthrombosis, and autoimmunity observed in Long COVID.

Acknowledgements: The experiments were conducted using research infrastructure purchased under Project Research Infrastructure Cell Technologies in Biomedicine (INFRAACT, Grant No. КП-06-Д1-12) of the national Roadmap for Research infrastructure. "Study of the excessive inflammasome mediated host tissue response inflicted clinically severe SARS-Cov-2 infection. Translation approach"

Investigating the influence of oxidised lipids and pathological biomarker amyloid-β (with sequences 1-42 and 42-1) on the membrane remodelling during Alzheimer's disease

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Keywords: *LUVs, (oxidised) lipids, amyloid-β peptides / oligomers, lipid order, ζ-potential*

Objective

The generation of **l**arge **u**nilamellar **v**esicle**s** (**LUVs**), characterized by a lipid profile like that of neuronal membranes in both norm and pathology (in the current case, Alzheimer's disease), along with investigation the influence of **amyloid-β** oligomers, plays a crucial role for establishing changes in the bilayer order (through the Generalized Polarization data) and membrane surface charge (i.e. ζ-potential), which are directly determined by intra- and intermolecular reorganization events among the lipophilic molecules. The **aim** is to considerate the impact of biophysical and biochemical alterations on the membrane order and the surface charge, when comparing **LUVs** with a lipid profile characteristic of a physiological state with one containing: **1.** oxidized lipid(s); **2.** amyloid-**β** oligomers. The **LUVs** were prepared by extrusion to mimic native and oxidatively modified neuronal membranes. Two physiologically relevant **OxPC** species (**POVPC** and **PGPC**), derived from lipid peroxidation, were incorporated into lipid bilayers. The effects of **$A\beta_{1-42}$** and reversed sequence of **Aβ** (**rAβ**, **$A\beta_{42-1}$**) peptides were examined on both control and **OxPC**-enriched **LUVs**. Membrane lipid order was quantified using **Laurdan** generalized polarization (**GP**) fluorescence spectroscopy, and surface charge (ζ-potential) was measured by electrophoretic light scattering. According to the **GP** values, the following effects are observed: **I. oxidised lipids** exert a more pronounced ordering impact; **II. amyloid-β** oligomeric forms further reduce membrane fluidity; **III. Aβ** and **rAβ in the presence of oxidised lipids synergistically** stiffened the membranes, increasing their negative surface charge, with the effect being more pronounced for **Aβ** oligomers. Regarding the ζ-potentials, there are measured significantly more electronegative values of the samples containing: **I. oxidised lipids**, likely due to the exposure of their polar group (aldehyde and / or carboxyl one) on the membrane surface, **II. Aβ** oligomers rather than **rAβ** ones, which is distinctive for the first three mixtures, III. PGPC that is explained through the deprotonated carboxyl group under physiological conditions.

ACKNOWLEDGEMENTS

The authors thank the: **1.** Bulgarian Ministry of Education and Science for support: The Scientific Infrastructure on Cell Technologies in Biomedicine (SICTB) D01-361/2023, **2.** National Centre for Biomedical Photonics D01-352/2023–part of the Bulgarian National Roadmap for Scientific Infrastructures 202 -2027, **3.** COST Action CA22153 EuroCurvoBioNet.

Differentiation of Primordial Germ Cell-like Cells from hESCs Using BMP-4 and hAFSC-4 Conditioned Medium

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Keywords: PGCLCs; human embryonic stem cells; BMP4; amniotic fluid stem cells; germline differentiation; conditioned medium

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Abstract

Objective:

This study aimed to establish a simple, reproducible, and cost-effective protocol for generating primordial germ cell-like cells (PGCLCs) from human embryonic stem cells (hESCs). The approach sought to mimic the physiological signaling of the embryonic germline niche by combining bone morphogenetic protein 4 (BMP4) stimulation with conditioned medium (CM) derived from SSEA4-positive human amniotic fluid stem cells (hAFSC-4).

Methods:

Human embryonic stem cells (line B1) were cultured under feeder-free conditions and induced with recombinant human BMP4 (50 ng/mL) in hAFSC-4 CM for 48 hours, followed by culture in CM alone for 14 days under adherent conditions. The hAFSC-4 CM was prepared from SSEA4-enriched amniotic fluid stem cells, whose secretome is rich in cytokines, growth factors, and extracellular vesicles relevant to germline specification. Cells were analyzed on day 14 post-induction by immunofluorescence for the germ cell markers VASA (DDX4) and DAZL.

Results:

Clusters of VASA- and DAZL-positive cells appeared as early as day 7 post-induction, increasing in number and size by day 14. The combination of BMP4 with hAFSC-4 CM significantly enhanced the efficiency and consistency of PGCLC generation compared to BMP4 treatment alone. The adherent culture system minimized variability associated with embryoid body formation, providing a controlled and reproducible microenvironment for germline induction.

Conclusion:

The established protocol successfully directed hESC differentiation toward a germline-like fate through synergistic BMP4 and hAFSC-4 secretome signaling. This method represents a physiologically relevant and reproducible in vitro model of human germline specification and differentiation, offering potential applications for studying infertility, epigenetic reprogramming, and germline-associated disorders. Future work should explore the molecular mechanisms underlying this differentiation process and assess the developmental potential of the derived PGCLCs toward functional gametogenesis.

ACKNOWLEDGMENTS

This study was funded by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project SUMMIT BG-RRP-2.004-0008-C01.

The role of HMGB1/RAGE interaction in driving epithelial-to-mesenchymal transition and invasion in breast cancer models

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Key words: EMT (epithelial-mesenchymal transition), HMGB1, RAGE, Breast cancer, NF-κB

High Mobility Group Box 1 (HMGB1) is a widespread nuclear protein. It can bind to DNA and is involved in many DNA-dependent processes. On the other hand, once secreted into the extracellular matrix, HMGB1 interacts with the transmembrane receptors and activates biochemical pathways related to carcinogenesis and metastasis. Of particular interest is its interaction with receptor for advanced glycation end products (RAGE). This interaction has been shown to be essential for inducing epithelial-mesenchymal transition (EMT) in triple-negative breast cancer. When HMGB1 binds to RAGE, it activates downstream signaling cascades, that inhibit epithelial markers while increasing mesenchymal marker expression, and respectively cells' invasive and migratory ability. This mechanism promotes metastasis and resistance to treatments. In our study we observed that HMGB1-induced EM-cell transition and increased breast cancer cell migration depend on RAGE expression. Targeted knockdown of RAGE using siRNAs led to a decreasing of cancer cells movement. Moreover, a decrease in the amount of extracellular HMGB1, also leads to inhibition of cells movement. Recently, this protein may prove to be a biomarker and target molecule for developing new cancer treatment strategies.

Acknowledgement: This project is funded by Bulgarian National Scientific Fund, project №: КП-06-Н51/13

Association studies of genes encoding receptors and ligands in patients with diabetes types 1.

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Keywords: diabetes, genes, KIR, HLA, biomarker

Abstract

Diabetes is one of the most dreaded diagnoses and unfortunately is still an incurable disease. Although the causes are not yet clear, association studies over the past two decades have shown that genetic imbalance between the killer immunoglobulin-like receptors (KIRs) on NK cells and their HLA class 1 ligands can enhance T-cell activation, which contributes to the pathogenesis of type 1 diabetes (T1D). The main goal of this study is to assess the impact of genes, encoding receptors and their ligands and their interaction, on the etiology and risk of developing T1D and potentially identify genomic biomarkers. To accomplish this task, DNA from patients with T1D and control subjects is extracted and the samples are genotyped (16 KIRs, HLA-C allele groups, HLA-B27 allele) using the PCR-SSP method. Based on publications and research, we assume that there is a relationship between the differences in haplotype and genotype of patients diagnosed with T1D and that of healthy controls. The results might shed light on the genetic factors, contributing to the development of autoimmune diabetes and also identify key biomarkers, which can be used to determine genetic predisposition.

Immunological Profile, Inflammatory Biomarkers, and Autoimmune Features of Post-COVID-19 Syndrome: a Bulgarian observational prospective study

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Keywords: post-covid, antinuclear antibodies, autoantibodies, inflammation, symptoms

Objective

This study included 60 participants whose demographic and clinical characteristics were analyzed to explore post-COVID-19 symptom persistence and associated laboratory parameters and autoantibodies.

Methods

Antinuclear antibodies (ANA) were determined by indirect immunofluorescence (IIF), and specific autoantibodies were detected using the EUROLINE ANA Profile 23 (EUROIMMUN, Germany) in serum samples. The fluorescence pattern analysis was performed under a fluorescence microscope by an experienced (>15 years) operator and classified according to the international ICAP nomenclature.

Results

Thirty-one patients (51.7%) were men, mean age of 58.98 ± 15.45 years (22–82), and mean BMI 25.93 ± 3.62. Sixteen patients (26.7%) experienced severe disease. The most frequent post-COVID symptoms were fatigue (50%), dyspnea (41.7%), sweating (40%), cough (36.7%), alopecia (36.7%), and sleep disturbances (31.7%), headache (30%), anxiety (28.3%), brain fog (26.7%), tachycardia (26.7%), low-grade fever (25%), joint and muscle pain (25%), palpitations (23.3%), dry mouth/throat (21.7%), and depressive episodes (21.7%). The mean CRP value was 9.94 ± 7.32 mg/L (0.50–33.20). Twenty-seven patients (45%) tested positive for ANA as follows: 1:80 (11 individuals),1:160 (6),1:320 (4), 1:640 (3), and ≥1:1200 (3), and 55 individuals (91.6%) showed positive cytoplasmic fluorescence (1:80-1:640). Among the ANA-positive patients, autoantibodies were detected against the following antigens: Mi2β [AC-4], PM-Scl75 [AC-8], RP11 [AC-10], RP155 [AC-10], dsDNA [AC-1], Ro-52, RNP/Sm [AC-5], Sm [AC-5], SS-B [AC-4], Ku [AC-4], PCNA [AC-13], Scl-70 [AC-29], gp210 [AC-11], DFS70 [AC-2].

Conclusions

Our findings suggest that post-COVID-19 symptoms are prolonged and multisystemic, with persistent fatigue and respiratory complaints being most prevalent. Mild elevations in inflammatory markers indicate a sustained low-grade inflammatory state, and high prevalence of autoantibodies, underscoring the need for long-term monitoring and rehabilitation strategies in post-COVID care.

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