16-18 APRIL 2026

THE FIRST PLEVEN SYMPOSIUM OF REGENERATIVE AND TRANSLATIONAL MEDICINE

Medical University – Pleven, Bulgaria

Index

Welcome

Dear Participants of "The First Pleven Symposium on Regenerative and Translational Medicine"

We are delighted to welcome you to the first Symposium held at the Medical University of Pleven. The Symposium on Regenerative and Translational Medicine, organised by Pleven Medical University, brings together international specialists to share and debate progress in stem cell science, biomaterials, mechanotransduction, and strategies for translating research into clinical care. Special attention will be given to how stem cells are used in regenerative therapies, especially their promise in tackling issues related to aging, diabetes, and tissue repair. These gatherings highlight our scientific community's commitment to exchanging ideas and promoting the application of foundational discoveries in clinical settings. We are proud to host distinguished speakers who have made significant impacts in their fields and possess extensive experience. Additionally, emerging scientists with notable achievements in specific disciplines are invited to participate. The Symposium is designed as an open forum for scientific discussion. Attendees can look forward to a social gathering after the opening session, an evening event, and a rapid-fire poster session, providing opportunities for participants to showcase their research and engage with colleagues and seasoned experts. Conveniently, coffee breaks are set near the poster displays to facilitate ongoing poster viewing throughout the conference. We trust you will find the program engaging and enjoy the vibrant atmosphere offered in this historic setting. We wish you an unforgettable stay at the First Symposium on Regenerative Medicine at the Medical University Pleven!

On behalf of the Scientific Committee

SCIENTIFIC COMMITTEE

Abhay Pandit, CÚRAM, University of Galway, IR

George Altankov, Center of Competence "Leonardo da Vinci", Medical University Pleven, BG

João Mano, CICECO – Aveiro Institute of Materials, University of Aveiro, PT

Regina Komsa-Penkova, Medical University Pleven, BG

Thomas Groth, Martin Luther University Halle-Wittenberg, DE

ORGANIZING COMMITTEE

Thomas Groth, Martin Luther University Halle-Wittenberg, DE

Regina Komsa-Penkova, Medical University Pleven, BG

George Altankov, Center of Competence "Leonardo da Vinci", Medical University Pleven, BG

Daniela Georgieva, Medical University Pleven, BG

Lora Topalova, Institute of Biophysics and Biomedical Engineering, BAS; Medical University Pleven, BG

Tanya Stoyanova, Institute of Biophysics and Biomedical Engineering, BAS; Medical University Pleven, BG

Oral presentations

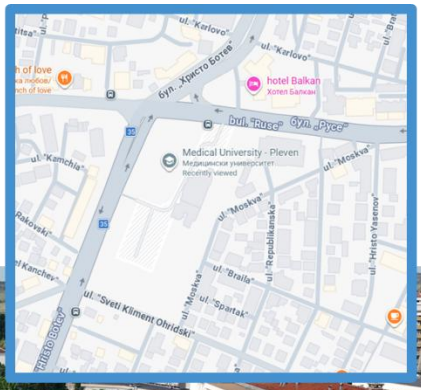
Speakers are requested to submit their PowerPoint presentations on a USB stick to the organizers at the reception desk on the previous day or at least two hours before their sessions begin. Regular oral presentations last 20 minutes, consisting of 17 minutes for the presentation and 3 minutes for discussion. Rapid-fire poster presentations are limited to 5 minutes and a maximum of 4 slides.

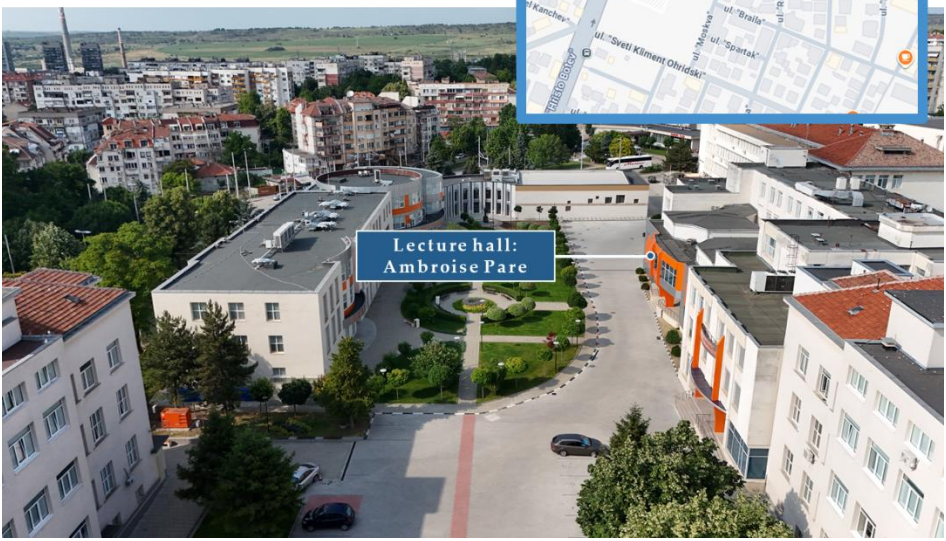
Poster Sessions

Poster sessions take place in the Ambroise Paré Lecture Hall foyer during coffee breaks. Posters should be 60 x 90 cm and must be mounted on April 16 before the opening session. Posters can be viewed throughout all coffee breaks.

Venue

Medical Univeristy Pleven, Kl. Ohridski Str. 1,
Pleven, Bulgaria
Lecture hall: Ambroise Pare





Medical University – Pleven

Established in 1974



https://www.mu-pleven.bg/

MU-Pleven Campus

Medical University – Pleven is one of Bulgaria's five state medical universities. Founded in 1974, it grew from the City Hospital of Pleven established in 1865, and has since evolved into a comprehensive academic, clinical, and research institution that educates students from over 45 countries.

Academic Programs & Structure

The University comprises five faculties: Medicine, Pharmacy, Public Health, Healthcare, and Veterinary Medicine, plus a Medical College. It offers 15 specialties across 5 master's and 10 bachelor's programs in 6 professional fields. In 1997, MU-Pleven became the first Bulgarian medical university to introduce English-language medical education. The University Hospital has over 1,000 beds and clinics covering all major medical specialties, along with specialized research units.

Innovation & Digital Medicine

MU-Pleven is a pioneer in advanced medical technologies. In 2007, the first Educational Experimental Center for Endoscopic Surgery opened in the Balkans. Its digital portfolio includes 3D printing and bioprinting laboratories, a virtual reality surgical training center, telepathology and telemedicine systems, holographic and augmented reality studios, and the Lecturio platform featuring 6,500 video lectures and 400 interactive 3D anatomy models developed by professors from Harvard, Yale, and Johns Hopkins.

Competence Center "Leonardo da Vinci"

Established in 2018 through EU co-financing, the Center unites MU-Pleven, Medical University Varna, and the Bulgarian Academy of Science (BAS) Institute of Robotics across 10 specialized laboratories for personalized medicine, 3D and telemedicine technologies, minimally invasive surgery, and robotic-assisted surgery using the Da Vinci Xi system, positioning MU-Pleven as a leading research platform in Southeastern Europe.

Pleven, Bulgaria

The City of History, Culture & Science of Northern Bulgaria


Panorama "Pleven Epic 1877"


City Hall


St George the Conqueror Chapel Mausoleum

Pleven is the seventh most populous city in Bulgaria, the administrative centre of Pleven Province, and the largest economic hub of Northwestern Bulgaria. With a population of approximately 90,000 (2021 census), it is an important cultural, scientific, and historical centre.

History

The Pleven region has been inhabited since the 5th millennium BC. Thracian cultures flourished here for millennia before the area became part of the Roman province of Moesia, where the road station Storgosia arose. The city gained international prominence during the Siege of Plevna (1877), a decisive episode in the Russo-Turkish War of Liberation that led to Bulgaria's independence from Ottoman rule, an event still celebrated annually through commemorations and reenactments.

Nature

Kaylaka Park, south of the city centre, is a 10,000-acre protected nature reserve in a karst valley carved by the Tuchenitsa River. It features rare flora and fauna listed in the Red Book of Bulgaria, sheer cliffs for rock climbing, artificial lakes, a zoo, a wine museum, and a restaurant built inside a natural cave. The Area Chernelka, 12 km from Pleven, offers a picturesque karst canyon rich in prehistoric Bronze Age finds.

Culture & Landmarks

Pleven's rich heritage includes: the Panorama "Pleven Epic 1877" , a monumental museum among Bulgaria's 100 National Tourist Sites; Skobelev Memorial Park with the House-Museum of Tsar Liberator Alexander II; the Regional Historical Museum (180,000+ exhibits); the Art Gallery "Iliya Beshkov" and the Svetlin Rusev Donative Collection; the Ivan Radoev Drama Theatre (est. 1919); and the Church of St. Nicholas (1834) , the oldest preserved church in Pleven and a national monument of the Bulgarian Renaissance.

Program

16th April THURSDAY

9:00 **Registration**

11:00 **Official Opening Ceremony**

Opening Speakers
Prof. Dobromir Dimitrov – Rector, Medical University – Pleven, BG
Prof. George Altankov – Medical University – Pleven, BG
Prof. Thomas Groth – Martin Luther University Halle-Wittenberg, DE

11:30 **PLENARY LECTURE I: Speaking the Body's Language: Glyco-Functionalized Biomaterial Systems as Orchestrators of Regenerative Host Responses**
Abhay Pandit · University of Galway, IE

12:30 **Lunch Break**

SESSION I · Bioactive Materials & Cells ·
Chairperson: Abhay Pandit

14:00 **KEYNOTE: Polysaccharide-based bioactive films for directing cell activity in regenerative medicine**
Thomas Groth · Martin Luther University Halle-Wittenberg, DE

14:30 **KEYNOTE: Elastin-Inspired Biomaterials: From Molecular Microstructure to Translational Scaffolds** –
Christian Schmelzer · Fraunhofer Institute IMWS Halle, DE

15:00 **KEYNOTE: Polymeric Biomaterials: Versatile Systems for Multiple Medical Applications** -
María Rosa Aguilar de Armas · ICTP – Institute of Polymer Science and Technology, Madrid, ES

15:30 **KEYNOTE: Characterization of Stem Cell–Secretome-Integrated Hybrid PLCL Nanofibers: Implications for Regenerative Medicine** –

George Altankov · Medical University Pleven, BG

16:00 **Coffee Break**

SESSION II · Rapid Fire Presentation Session

16:30 Rapid Fire Presentations (5 min each)

P-01 **Histological Analysis of 3D Collagen Type I/II Constructs Displays Cartilage-Like Tissue Formation In Vitro.**

Cvetan Popov · Dept. of Anatomy, Histology, Cytology & Biology · Medical University Pleven, BG

P-02 **Poly(sulfobetaine methacrylate) Ionogels Synthesized via Direct Mixing: Emerging Drug Delivery Platforms.**

Denitsa Nikolova · Laboratory on Structure and Properties of Polymers, Faculty of Chemistry & Pharmacy, Sofia University 'St. Kliment Ohridski', Sofia, BG

P-03 **Beta Cell Regeneration During Long-Term Metformin Treatment in a HFD/STZ Rat Model of Type 2 Diabetes.**

Plamena Panayotova · Dept. of Pharmacology and Toxicology, Medical University Pleven, BG

P-04 **Circulating Histone Signatures in Plasma Reveal Distinct Profiles Across Solid Tumors and Myelodysplastic Syndrome.**

- Desislava K. Tsoneva · Medical University-Varna, Varna, BG

P-05 **Establishing an Optimized Protocol for Isolation and Culture of Wharton's Jelly–Derived Mesenchymal Stem Cells toward Comparative Secretome Studies in Normal and Preeclamptic Pregnancies.**

Rebecca Caiulo Dept. of Obstetrics & Gynecology, University Hospital 'Dr. Georgi Stranski', Pleven, BG

P-06 **Paracrine Signals from B-Cell Neoplasms Induce Reprogramming Toward a Cancer-Associated Phenotype in Stem Cells.**

Tanya Stoyanova Institute of Biophysics and Biomedical Engineering, BAS, Sofia, BG

P-07 **MicroRNA Profiling in Metastatic Melanoma.**

Iliyan Dimitrov Pochileev · Dept. of Medical Genetics, Medical University Sofia, Sofia, BG

P-08 **Secretome-Based Bioactive Dressing for Wound Regeneration and Improved Scar Quality In The Wistar rat model.**

Iren Bogeva-Tsolova, Department of Surgical Diseases, Department of Anatomy, Histology, Cytology, and Biology, Medical University Pleven, BG

SESSION III · Medical Application of Advanced Biomaterials

· *Chairperson: María Rosa Aguilar de Armas*

17:20 **Innovative Biomaterials and Emerging Biotechnologies in Wound Healing: Insights from a Surgeon**

Pencho Tonchev · Medical University Pleven, BG

17:40 **Paracrine Effects of Buccal Fat Pad–Derived Dedifferentiated Fat Cells on Bone and Cartilage Regeneration**

Svilen Angelov Medical School Charité Universitätsmedizin Berlin, DE

18:00 **A Translational Framework for Regeneration of Inferior Turbinate Erectile Tissue Using Injectable 3D Macroporous Hydrogel Scaffolds**

Boyan Donev · Hopewell Foundation, Sofia, BG

18:40 **Get-Together Welcome Party**
Foyer, Ambroise Paré Lecture Hall

17th April FRIDAY

SESSION IV · Advanced Biomaterials & Cells II ·

Chairperson: Thomas Groth

9:00 **KEYNOTE: Hyaluronan – A Simple Glycosaminoglycan with Multiple Functions –**

Iva Pashkuleva · 3Bs Research Group, University of Minho, PT

9:30 **KEYNOTE: Therapeutic siRNA-Guided Differentiation and Crosstalk in Bone Regeneration**
Michaela Schulz-Siegmund · University of Leipzig, DE

10:00 **Biomimetic Microgels in Tissue Regeneration and Disease Models –**
Jose Luis Gomez Ribelles · Polytechnical University of Valencia, ES

10:30 **KEYNOTE: 3D Bioprinting – High Hopes for Tissue Repair –**
Victoria Sarafian · Medical University Plovdiv, BG

11:00 **Coffee Break**

11:30 **PLENARY LECTURE II: Biomaterials with Distinct Levels of Cell Contents**
João Mano · University of Aveiro, PT

12:30 **Lunch Break & Poster Session**

14:00 **SPECIAL PRESENTATION: Competence Center 'Leonardo da Vinci': A Platform for Regenerative Medicine, Innovation, and Technology Transfer**
Dobromir Dimitrov · Rector, Medical University Pleven, BG

SESSION V · Mechanobiology & Stem Cells ·
Chairperson: George Altankov

14:20 **KEYNOTE: Mechano-Chemical Information in Cells and Emergent Properties in Multicellular Organisms –**
Yannis Missirlis · Aristotle University of Thessaloniki, GR

14:50 **KEYNOTE: Translating Tendon Biology into Regenerative Therapies -**
Denitsa Docheva · University of Würzburg, DE

15:20 **Uncovering the Biological Properties of Dental-Derived MesenchymalStem Cells –**
Nikolay Ishkitiev · Medical University Sofia, BG

15:40 **Mesenchymal Stem Cell Interactions with Glycated Collagen: Adhesion Dynamics, Mechanotransduction, and Matrix Remodeling –**
Regina Komsa-Penkova · Medical University Pleven, BG

16:00 **Coffee Break & Poster Session**

SESSION VI · Stem Cells, Bioprinting & Regenerative Therapies

· *Chairperson: Victoria Sarafian*

16:30 **Divergent Mitochondrial Responses to Palmitate-Induced Lipotoxic Stress: Image-Based Analysis of Network Dynamics and Membrane Potential in Two Main Adipose Tissue-Derived Cell Types –**
Antonina Gospodinova · Bulgarian Academy of Sciences, Sofia, BG

16:50 **A Multimodality Approach for the Treatment of High-Grade (III–IV) Burns: PRGF, Photobiomodulation, Cold Atmospheric Plasma –**
Nikolay Tzaribashev · Regenix, Sofia, BG

17:10 **Regeneration of Critical Bone Defects Using Bioprinted MSCs in a Mouse Model –**
Despina Pupaki, Institute of Biology and Immunology of Reproduction, BAS, Sofia, BG

17:30 Regenerative Strategies for Alopecia Using Platelet-Derived Exosomes
Radostin Aleksandrov · Medical University Pleven, BG

20:30 **Social Dinner | Hotel Balkan – 14th Floor, Panorama Restaurant**

18th April SATURDAY

SESSION VII · Bioprinting, Stem Cells & Regenerative Therapies

· *Chairperson: Jose Luis Gomez Ribelles*

9:00 **Collagen Substrate Remodeling as a Tool to Assess Paracrine Signaling Between B Cell Neoplasms and Stem Cells.**
Lora Topalova Institute of Biophysics and Biomedical Engineering, BAS, Sofia, BG

9:30 **Material Design Strategies for Advanced Biofabrication –**

Murat Redzep · Medical University Plovdiv, BG

9:50 **3D-Printed Bioreactor as a Model System for Artificial Cartilage Tissue** -
Cvetan Popov· Dept. of Anatomy, Histology, Cytology & Biology · Medical University Pleven, BG

10:10 **IL-8 as a Marker for Early In Vitro Education of Human Bone Marrow Mesenchymal Stem Cells by Multiple Myeloma Cell Lines** –
Nadia García-Parra · Polytechnic University of Valencia, ES

10:30 **Closing Ceremony & Farewell**

PRACTICAL COURSE · Hands-On Techniques in Regenerative Medicine

11:30 Practical Course – Part I
George Altankov · Murat Redzep · Regina Komsa-Penkova

13:00 **Basket Lunch**

13:30 Practical Course – Part II
George Altankov · Murat Redzep · Regina Komsa-Penkova

Posters list

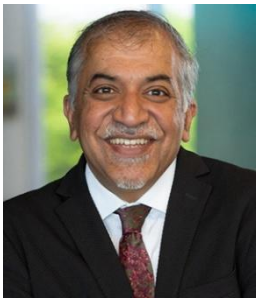
P-01	**Histological Analysis of 3D Collagen Type I/II Constructs Displays Cartilage-Like Tissue Formation In Vitro.** *Cvetan Popov · Dept. of Anatomy, Histology, Cytology & Biology · Medical University Pleven, BG*
P-02	**Poly(sulfobetaine methacrylate) Ionogels Synthesized via Direct Mixing: Emerging Drug Delivery Platforms.** *Denitsa Nikolova · Laboratory on Structure and Properties of Polymers, Faculty of Chemistry & Pharmacy, Sofia University 'St. Kliment Ohridski', Sofia, BG*
P-03	**Beta Cell Regeneration During Long-Term Metformin Treatment in a HFD/STZ Rat Model of Type 2 Diabetes.** *Plamena Panayotova · Dept. of Pharmacology and Toxicology, Medical University Pleven, BG*
P-04	**Circulating Histone Signatures in Plasma Reveal Distinct Profiles Across Solid Tumors and Myelodysplastic Syndrome.** *Desislava K. Tsoneva · Medical University-Varna, Varna, BG*
P-05	**Establishing an Optimized Protocol for Isolation and Culture of Wharton's Jelly–Derived Mesenchymal Stem Cells toward Comparative Secretome Studies in Normal and Preeclamptic Pregnancies.** - *Rebecca Caiulo · Dept. of Obstetrics & Gynecology, University Hospital 'Dr. Georgi Stranski', Pleven, BG*
P-06	**Paracrine Signals from B-Cell Neoplasms Induce Reprogramming Toward a Cancer-Associated Phenotype in Stem Cells.** - *Tanya Stoyanova · Institute of Biophysics and Biomedical Engineering, BAS, Sofia, BG*
P-07	**MicroRNA Profiling in Metastatic Melanoma.** *Iliyan Dimitrov Pochileev · Dept. of Medical Genetics, Medical University Sofia, Sofia, BG*
P-08	**Secretome-Based Bioactive Dressing for Wound Regeneration and Improved Scar Quality In The Wistar rat model.** *Iren Bogeva-Tsolova, Department of Surgical Diseases, Department of Anatomy, Histology, Cytology, and Biology, Medical University Pleven, BG*

P-09	**Prostate cancer stem-like phenotype is associated with enhanced immune evasion and therapeutic resistance.** *Andrey Velichkov · Institute of Biology and Immunology of Reproduction, Bulgarian Academy of Sciences, Sofia;*
P-10	**Electrospun Nanofibers Enriched with Cryoprecipitate as Bioactive Cell-Adhesive Matrices for Personalized Regenerative Medicine**. - *Borislav Dimitrov · Department of Chemistry/Biochemistry, MU-Pleven; Center of Competence in Personalized Medicine, 3D and Telemedicine, Robotic Assisted and Minimally Invasive Surgery - "Leonardo da Vinci", Pleven, BG*
P-11	**Astrocyte Metabolism and Their Role in Development of Neurodegenerative Diseases.** – *Gaudia Aghanenu · Faculty of Medicine, Prof. Dr. Assen Zlatarov State University of Burgas, 1 Prof. Yakim Yakimov Blvd., Burgas, BG*
P-12	**In Situ UV-Initiated Synthesis and Characterization of Polysulfobetaine/BMIM Iongels for Biomedical Applications.** – *Konstans Ruseva · University/Institution: Sofia University "St. Kliment Ohridski", Faculty of chemistry and pharmacy, Sofia, BG*
P-13	**Polymer/Calcium Phosphates Hybrid Materials as Dental Restoratives: An Exploratory Study**. *Marin Simeonov · Laboratory on Structure and Properties of Polymers, Faculty of Chemistry and Pharmacy, University of Sofia, Sofia, BG*
P-14	**Assessment of proliferation and osteogenic differentiation of bioprinted mesenchymal stem cells in GelXA BONE and CELLINK BONE bioinks.** *Snejana Kestendjieva · Institute of Biology and Immunology of Reproduction, Bulgarian Academy of Sciences, Sofia, BG*
P-15	**Impact of post-translational collagen oxidation and glycation on mesenchymal stem cell interaction and matrix remodeling.** ***Svetoslava Stoycheva** · Medical University Pleven, Department of Biochemistry; Center of Competence in personalized medicine, 3D and telemedicine, robotic assisted and minimally invasive surgery at Medical University Pleven, BG*
P-16	**Application of Electrochemotherapy in 3d Bioprinted Colorectal Cancer Models - a Pilot Study**. - *Tsvetomira Ivanova · Department of*

	Medical Biology, Medical University- Plovdiv; Research Institute at Medical University-Plovdiv, Plovdiv, BG
P-17	**A murine embryonic fibroblast model to study the etiology of Rahman syndrome.** *Veliko Nikolov Kostadinov · Institute of Molecular Biology, Bulgarian Academy of Sciences, Sofia, BG*
P-18	**Isolation and Functional Assessment of Jellyfish-Derived Biomaterial. -** *Violina Ivanova · Medical University Pleven, Department of Biochemistry; Center of Competence in Personalized Medicine, 3D and Telemedicine, Robotic Assisted and Minimally Invasive Surgery, Medical University Pleven, BG*
P-19	**Applications of 3D Printing and Medical Image Segmentation in Surgical Planning and Training**. *Vladislav Hristov · Center of Competence in Personalized Medicine, 3D and Telemedicine, Robotic Assisted and Minimally Invasive Surgery – "Leonardo da Vinci"; Medical University Pleven, Pleven, BG*
P-20	**Application of Collagen-Based Bioinks for Chondrocyte Differentiation in 3D Bioprinted Human Stromal-Vascular Fraction (SVF) Cells – Comparative Gene Expression Analysis** *Yordan Sbirkov · Dept. of Dialysis Treatment, St George University Hospital, Plovdiv, BG*
P-21	**Differential Caspase-1 Activation Induced by SARS-CoV-2 ORF3a Mutants Reveals Variant-Dependent Inflammasome Signaling in Human Endothelial Cells** *Yuliia Ilieva · Institute of Biology and Immunology of Reproduction, BAS, Sofia, BG,*
P-22	**Optimizing AD-MSC Isolation from Lipoaspirates for Translational Medicine: A Comparative Pilot Study** *Bozhidar Vergov · Medical University Plovdiv, BG*
P-23	**Artificial Intelligence-Assisted Monitoring of Induced Pluripotent Stem Cell Cultures for Standardised Regenerative Medicine** *Remon Hanna · King's College Hospital NHS Foundation Trust, GB*

Plenary Speakers

Prof. Abhay Pandit



Professor Abhay Pandit is the Established Professor in Biomaterials and Founding Director of a Research Ireland Centre for Research in Medical Devices (CÚRAM) hosted at the University of Galway. Professor Pandit's research focuses on utilising glycosylation patterns from human pathological disease states to develop innovative strategies for modulating these states using biomaterials. These biomaterials have a high payload capacity, programmable degradation profiles, and incorporate gradients of physical, chemotropic, and protective cues, allowing for the sustained delivery of multiple biomolecules to target injury mechanisms at the molecular and cellular levels. Professor Pandit's research emphasises the application of glycobiology in this field. He is the author of 28 patents and has licenced four technologies to medical device companies. He has published over 350 manuscripts in esteemed journals, including Science Translational Medicine, PNAS, Science Advances, Nature Communications, Biomaterials, and other notable high-impact publications. He has been honored with the esteemed George Winter Award 2022, the Chandra P Sharma Award 2023, and the Biomaterials Advances Innovation Award 2023 for his research contributions to biomaterials. He is also a fellow of the American Institute for Medical and Biological Engineering (AIMBE), Tissue Engineering and Regenerative Medicine International Society (TERMIS), Irish Academy of Engineering, Royal Irish Academy, and International Union of Societies for Biomaterials Science and Engineering (IUSBSE). He is currently the President Elect of TERMIS (Global).

Prof. João F. Mano

João F. Mano is a Full Professor at the Chemistry Department of University of Aveiro, Portugal. He combines advanced biomaterials and cells towards multidisciplinary concepts in the field of regenerative and personalized medicine. Specifically, he utilizes biomimetic and nano/micro-technology approaches to develop polymer-based biomaterials for the creation of biomedical devices with enhanced structural and multi-functional properties. He also engineers microenvironments to regulate cell behavior and organization, with the goal of clinically applying these technologies in advanced therapies or in the bioengineering of disease models. He serves as the Editor-in-Chief of Materials Today Bio (Elsevier). He has been coordinating multiple research projects, including 2 Advanced Grants, 1 Synergy Grant, and 3 Proof-of-Concept Grants from the European Research Council. He received different honours, including two honoris causa doctorates (Univ. of Lorraine and Univ. Utrecht), the George Winter Award 2020 from the ESB and he was elected fellow FEurASc, FBSE and FAIMBE.

Keynote Speakers

Prof. Thomas Groth

Thomas Groth is Professor Emeritus of Biomedical Materials at Martin Luther University Halle-Wittenberg and former Director of the Department of Biomedical Materials. He was a board member of the Interdisciplinary Center of Materials Science and spokesperson for the International Graduate School AGRIPOLY at Martin Luther University. He also served for several years as an Adjunct Professor at the I.M. Sechenov Medical University in Moscow. From 2015 to 2017, he was President of the European Society for Artificial Organs (ESAO), one of the world's largest societies in the field of artificial organs, and in 2023 received the Emil Bücherl Prize from the ESAO for his outstanding contributions to the field of artificial organs and regenerative medicine. During his scientific career, he made significant contributions to understanding the biocompatibility of biomaterials, was actively involved in the development of membranes for bioartificial organs and worked on material developments for tissue engineering of skin and bone. His scientific work is represented by more than 250 publications and 15 patents in the fields of biomaterials science, membrane technology and tissue engineering.

Prof. Christian Schmelzer

Christian Schmelzer is Interim Institute Director at the Fraunhofer Institute for Microstructure of Materials and Systems (Fraunhofer IMWS, Germany) and Head of the department "Biological and Macromolecular Materials." His research focuses on extracellular-matrix–inspired biomaterials for regenerative and translational medicine, with a particular emphasis on elastin and elastic fibers. For more than two decades, he has investigated elastin structure–function relationships, including post-translational modifications, cross-linking chemistry, and aging-related changes, and how these factors affect molecular assembly, microstructure, and bioactivity. Building on this mechanistic understanding, he develops functional elastin-based materials such as tunable hydrogels, electrospun fibers, and crosslinked scaffolds designed for soft-tissue repair and regenerative microenvironments. His group combines biomaterials engineering with advanced microstructure characterization and proteomics/mass spectrometry to analyze ECM composition, modification patterns, and elastin-derived peptides relevant to tissue remodeling and degeneration. He is also a co-founder of a spin-off translating medical-grade elastin materials toward practical applications.

Prof. María Rosa Aguilar

Dr. María Rosa Aguilar received her PhD in chemistry from Universidad Complutense de Madrid in 2002 working on polymeric biomaterials. She has been postdoc at University of Brighton and performed scientific stays at UCL (UK), University of Washington (USA) and ESRF (France). She is Scientific Researcher of the CSIC at the Institute of Polymer Science and Technology (ICTP-CSIC), where she currently carries out her research activity. Her group works in two main research lines: synthesis and characterization of advanced delivery systems; and polymeric scaffolds for tissue engineering. Her work is strongly translational, bridging fundamental polymer science with clinical needs through close collaboration with medical device and pharmaceutical companies.

Dr. Aguilar has published more than 100 research papers and is editor of the two editions of the book "Smart Polymers and their Applications". Moreover, she is Deputy Scientific Director of CIBER-BBN, a national network of Excellence working on Biomaterials, Bioengineering and Nanomedicine; she is also member of the Governing Board and Treasurer of the Specialized Group of Polymers (GEP) from the Spanish Royal Society of Physics and Chemistry (RSEFQ); and member of the Governing Board of the Interdisciplinary Platform of CSIC for Sustainable Plastics towards a Circular Economy (SUSPLAST+).

Prof. George Altankov

Prof. George Altankov received his MD in 1974 from the Varna Medical Institute, Bulgaria, where he also completed his PhD in 1984. Between 1991 and 1993, he pursued postdoctoral studies at the Southwestern Medical School in Dallas, focusing on the molecular mechanisms of cell adhesion.

From 1985 to 2005, he worked at the Bulgarian Academy of Sciences, advancing to Full Professor, Head of the Department Cell Adhesion, and Deputy Director of the Institute of Biophysics in Sofia. His pioneering studies, conducted in close collaboration with the GKSS Research Centre (Germany), were among the first to demonstrate that tissue compatibility of biomaterials strongly depends on the ability of cells to reorganize surface-associated extracellular matrix proteins such as fibronectin, vitronectin, fibrinogen, and collagen.

From 2007 to 2019, Prof. Altankov held the distinguished position of ICREA Research Professor at the Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain, leading the group "Molecular Dynamics at the Cell–Biomaterials Interface" consequently leading 3 EU funded research projects in the field of tissue engineering and regenerative medicine.

Upon returning to Bulgaria in 2019, he continued his scientific activity, initially as a consultant and later as a work package leader in the development of the Leonardo da Vinci Center of Competence in Personalized Medicine, 3D and Telemedicine, Robotic and Minimally Invasive Surgery at Pleven Medical University. He currently holds a leading role in project BG16RFPR002-1.014-0002-C001 within the same Center of Competence. His research is further supported by the European Union's NextGenerationEU program through the National Recovery and Resilience Plan of the Republic of Bulgaria (project BG-RRP-2.004-0003).

Prof. Altankov is the author of more than 150 original research papers in international journals and over four book chapters, with his work cited more than 3,500 times (Google Scholar, h-index = 36). He is also the holder of five patents.

Iva Pashkuleva, PhD

Iva Pashkuleva is a Principal Investigator at 3Bs Research Group, University of Minho, Portugal. She holds PhD in Organic chemistry from University of Sofia, Bulgaria (2000) and works at the interface of carbohydrate and supramolecular (non-covalent) chemistry towards development of biomimicking systems that aid the understanding and the treatment of different pathologies. The design of specific glycan copolymers and amphiphiles as well as their self-assembly at physiological conditions or in response to physiological stimuli plays a central role in her research. The developed supramolecular systems are used to gain fundamental insights into extracellular matrix organization, dynamics and function as well as to design adaptive and responsive biomaterials.

Iva Pashkuleva is an author of more than 100 publications focused on the development of new analytical methods and platforms for characterization of challenging to measure glycan-protein and glycan-cell interactions; glycan-based delivery systems; selective cancer therapies based on biocatalytic self-assembly of glycan amphiphiles; and extracellular supramolecular mimics.

She has been awarded several prestigious grants for her research - a Starting Grant (2008) and two Consolidator Grants (2013 and 2019) from the Portuguese scientific foundation. Currently, she participates in several European consortia that develop clinical solutions for different pathologies such as diabetic foot ulcers and neonatal intensive care.

Prof. Michaela Schulz-Siegmund

Michaela Schulz-Siegmund is a pharmacist by training. She received her doctorate in Pharmaceutical Technology at the University of Regensburg, Germany. From 1997 to 2003, she was a research assistant in Prof. Göpferich's group at the University of Regensburg and qualified as a professor in 2004. During this time, she spent a research stay with Prof. Mikos at Rice University, Houston, Texas. 2003-2006 she was a visiting/contract professor of Pharmaceutical Technology at the Karl-Franzens-University in Graz, Austria. Since 2007 she is full professor of Pharmaceutical Technology at Leipzig University. Since 2010, she is head of the Institute of Pharmacy in Leipzig. Michaela Schulz-Siegmund was president of the German Chapter of the Controlled Release Society 2019/20. She is Head of the Saxonian Chapter of the German Pharmaceutical Society. She is currently an elected member of the German Research Foundation (DFG) review board.

Her major research fields are biomaterial design for tissue engineering and controlled release systems for nucleic acids. Her focus in bone tissue engineering is on human mesenchymal stem cells and siRNA as a tool to control differentiation. She is also interested in siRNA transfection systems, including stabilized Calcium Phosphate Nanoparticles and Extracellular Vesicles.

Prof. Yannis Missirlis

Professor Yannis Missirlis graduated as Chemical Engineer from the NTUA (Athens-1969), received a M.Sc in Chemical Engineering, (Syracuse-USA, 1971) and his Ph.D. from Rice University (Houston-1973) in Biomedical Engineering.
Prof. Missirlis was Assistant /Associate Professor at McMaster University (Canada,1974-1980) before joining the University of Patras in 1981, as a full Professor, directing since then the Laboratory of Biomechanics and Biomedical Engineering, until his retirement (1/9/2013).
Prof. Missirlis has served as Vice-Rector of the University (1986-1988), as a member of the European, and the World Council of Biomechanics.

He is an Honorary Member of European Society of Biomechanics, and of the ESB (Biomaterials). In 2019 he was elected a Fellow of Biomaterials Science and Engineering (FBSE). He has coauthored a textbook: "Biomaterials, A Tantalus Experience"(Helsen-Missirlis, 2011), coedited 2 books: " Modern aspects of Protein Adsorption on Biomaterials" (Missirlis-Lemm, 1991) and " The role of Platelets in Blood- Biomaterial Interactions" (Missirlis-Wautier, 1993).

He has published >90 peer-reviewed papers in international journals, several chapters in books, and currently is active in the area of cell-material interactions, mechanotransduction, tissue engineering, biomechanics from nano-to macro level, mechano-epigenetics.

Prof. Missirlis is currently a SUNUM Affiliated Researcher (Sabanci University Nanotechnology Center, Istanbul, Turkey), and Collaborator of the LTFN Laboratory at Aristotele University of Thessaloniki, Greece.

Prof. Denitsa Docheva

Prof. Dr. Denitsa Docheva Department of Musculoskeletal Tissue Regeneration Orthopaedic Hospital König-Ludwig-Haus (KLH) University of Würzburg Würzburg, GERMANY Denitsa graduated with two parallel Master Degrees (Biology and Chemistry) from the Paisii Hilendarski University of Plovdiv, Bulgaria. Afterwards Denitsa obtained a PhD fellowship at the Max-Planck-Institute of Biochemistry, Martinsried, Germany and graduated in 2005. Then she moved to the Department of Trauma Surgery, Ludwig-Maximilians-University (LMU) in Munich, Germany where she established the Tendon Research Group. In 2012, Denitsa completed her habilitation in Experimental Surgery at the LMU. 2016 to 2021, she was Professor for Experimental Trauma Surgery and Research Director at the Department of Trauma Surgery, University of Regensburg, Germany. In October 2021, she became Professor and Chair of the Department of Musculoskeletal Tissue Regeneration, KLH & University of Würzburg, Germany. She has published more than 100 articles and has won multiple grants; currently, she is participating in several EU consortia (MEFISTO, OSTEOMET, OSTASKILLS, NetwOArk and TENET). 2018 to 2020, she was the President of the European Orthopaedic Research Society (EORS). 2018 to 2022, she served at the steering committee of the International Combined Orthopaedic Research Society (ICORS). 2019 to 2023, she was the Chair of the Musculoskeletal Regeneration Network of the Basic Research Section of the German Society of Orthopaedic and Trauma Surgery (DGOU). 2022, she was recognized as a Fellow of International Orthopaedic Research (FIOR) by ICORS and was awarded the Commemorative Medal of the University of West Bohemia, Pilsen, Czech Republic. Since 2023, she is a member of the International Advisory Board "Strategic Research and Innovations Program" Medical University – Plovdiv, Bulgaria.

Prof. Victoria Sarafian

Professor Victoria Sarafian was graduated from the Faculty of Medicine at Medical University of Plovdiv, Bulgaria.
Postdoctoral fellow at the universities of Cambridge (UK), Nantes (France), and Namur (Belgium) in molecular immunology, cellular and molecular biology. Specialist in medical biology and in clinical immunology.
Acted as Vice-Rector for Research, Head of the Department of Medical Biology and Director of the Research Institute at Medical University of Plovdiv. Head of the Division of Molecular and Regenerative Medicine. Leader and coordinator of national and international research projects, member of editorial boards, reviewer for several scientific journals, and invited national and international guest lecturer. Research interests in the field of translational medicine, bioprinting and molecular biomarkers.

Assoc. Prof. Nikolay Dimitrov Ishkitiev

Ivan Ishkitiev is an Associate Professor in the Department of Medical Chemistry and Biochemistry at the Medical Faculty of Medical University – Sofia, a position he has held since 2025. He graduated with a DDS degree from the Faculty of Dentistry, Medical University – Sofia, in 2002, after which he entered private dental practice until 2008. His academic career began that same year as a researcher in the Department of Medical Chemistry and Biochemistry at Medical University – Sofia, where he was simultaneously enrolled as a PhD student funded by the Ministry of Education, Youth and Science grant UB-404/06 under the Programme "Development of the Scientific Potential" (2006–2010). In parallel, he undertook a second doctoral training at the Department of Oral Health, Nippon Dental University, Tokyo, Japan (2009–2013), graduating in September 2013, and completed his Bulgarian doctorate in May 2014.

Between 2013 and 2015 he served as Assistant Professor and Specialist in Pediatric Dentistry at the Faculty of Dental Medicine, Medical University – Sofia. In 2015, he returned to the Department of Medical Chemistry and Biochemistry as an Assistant Professor, was promoted to Chief Assistant Professor in 2016, and advanced to his current rank of Associate Professor in 2025. His scientific interests bridge biochemistry and dental medicine, with a focus on stem cell biology, extracellular matrix biochemistry, and the molecular mechanisms of oral health and disease. He brings over two decades of combined clinical, research, and teaching experience to his current role.

Abstracts

Invited Lectures

Biology-First Biomaterial Design: Reading Disease Molecular Signatures

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The biomaterials field stands at an inflection point, and the most consequential shift underway is not a new material or fabrication technique — it is a fundamental change in starting point. For too long, biomaterial design has begun with the material and asked how biology might respond to it. The paradigm we advocate inverts this logic: begin with the disease, read its molecular signature, and let that signature dictate the therapeutic design. This patient-stratified, biology-first philosophy is not the exclusive domain of any single omics discipline. The molecular fingerprints of pathological tissue can be decoded through the glycome, the lipidome, the metabolome, or the transcriptome — each offering a different but complementary window into how disease reshapes the cellular and extracellular environment. We call on the broader biomaterials community to embrace this approach: to ask first what the diseased tissue is saying at a molecular level, and then to design materials that respond to that signal with precision. Our group has pursued this philosophy through the lens of glycobiology — an area uniquely underexploited in biomaterial design despite glycans being the most structurally diverse and abundant macromolecules on the cell surface. Through patient-stratified glycomic profiling, we identify the aberrant glycosignatures — dysregulated sialylation, fucosylation, and glycosaminoglycan remodelling — that perpetuate chronic inflammation and impair repair. Our biomaterial systems are designed not to add biological activity generically, but to suppress these specific pathological displays, shifting the microenvironment from disease-sustaining to regeneration-permissive. The self-organising capacity of glyco-functionalised supramolecular assemblies further enables hierarchical architectures that recapitulate native tissue organisation with a fidelity that conventional functionalisation strategies cannot match. This is one realisation of a broader vision: that the biomaterials field, whichever molecular language it chooses to read — glycomic, lipidomic, metabolomic — must start from disease

biology and design outward, letting the body's own signals define the therapeutic strategy.

Acknowledgments

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Polysaccharide-based bioactive films for directing cell activity in regenerative medicine

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Conventional implants and tissue engineering scaffolds composed of synthetic materials for the replacement of musculoskeletal or other tissues frequently exhibit surface chemistry that often fails to elicit the optimal tissue response. Therefore, surface coatings on implants inspired by elements of the extracellular matrix (ECM) can be utilised to accurately regulate cell activity and consequently influence the healing process. Glycosaminoglycans (GAGs) exhibit notable bioactivity owing to their substantial affinity for numerous proteins, which constitute both soluble and insoluble components of the ECM (e.g. growth factors, fibronectin). Furthermore, GAGs directly interact with cell receptors responsible for regulating cellular fate (e.g. hyaluronan receptor CD44). However, the development of surface coatings for implants utilizing natural or semisynthetic GAG necessitates distinct approaches for covalent or physical attachment. Physical immobilization using the layer-by-layer (LbL) technique can take advantage of the natural charge of GAGs (negatively charged), as well as proteins such as collagen and polysaccharides like chitosan (positively charged depending on pH value), allowing for the creation of multilayers held together by ion pairing. Additionally, intrinsic covalent cross-linking of activated GAGs with the pendant groups of the other polyelectrolytes (e.g. chitosans amino group) can be utilized. This presentation will highlight our accomplishments in manipulating the cellular microenvironment through multilayer systems designed to regulate osteogenic and chondrogenic differentiation of mesenchymal stem cells. Furthermore, we will illustrate the utility of these multilayer systems as effective platforms for the storage and delivery of growth factors such as BMP-2, which facilitate osteogenic differentiation of cells. Stimuli-responsive intrinsic cross-linking through imine bond formation is particularly important in this context. Ternary systems loaded with trace metal ions can guide cell differentiation toward osteogenesis by using multilayers that store and release these ions to induce mesenchymal stem cell differentiation. Additionally, embedding liposomes and lipoplexes enables in-situ delivery of drugs or plasmid DNA to program stem cells for osteogenic differentiation. We will also show that the LbL technique can be used to create not only thin coatings but also free-standing multilayer films. Additionally, we will demonstrate that cross-linking processes do more than enhance mechanical strength; they can also boost the bioactivity of these freestanding films toward human

dermal fibroblasts also by loading with fibroblast growth factor FGF-2, making them suitable for use as wound dressings.
To sum up, these biomimetic surface coatings or free-standing films act as a toolbox for precisely controlling cell responses. This approach could lead to smart, cell-instructive coatings for implants, tissue engineering scaffolds and wound dressings.

Elastin-Inspired Biomaterials: From Molecular Microstructure to Translational Scaffolds

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Elastic fibers are essential extracellular matrix components that provide elasticity and recoil to tissues such as skin, lung, and the vasculature. Their unique durability arises from the hierarchical assembly of tropoelastin on fibrillin-rich microfibrillar templates, followed by enzymatic cross-linking into a stable, highly extensible polymer network. Despite their longevity, elastic fibers are not immutable: aging and disease progressively alter elastin microstructure through proteolysis, oxidative damage, glycation, calcification, and mechanical fatigue, ultimately reducing tissue compliance and contributing to pathology.

This contribution links key molecular and microstructural features of elastin-self-assembly/coacervation behavior, cross-link architecture, and biologically active sequence motifs- to macroscopic material properties and cell response. Based on these design principles, we present elastin-inspired biomaterial platforms ranging from electrospun fibrous meshes to printable hydrogel systems and composite scaffolds, aiming to reproduce soft-tissue mechanics while enabling controlled remodeling. Emphasis is placed on how tuning cross-link density, viscoelasticity, and degradation kinetics can tailor performance for specific regenerative indications.

Polymeric Biomaterials: Versatile Systems for Multiple Medical Applications

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Short Background: Polymeric biomaterials provide a versatile platform for developing advanced therapeutic systems in regenerative medicine and drug delivery. Their tunable physicochemical properties and capacity for molecular modification make them ideal for addressing complex clinical needs. This keynote highlights three representative technologies from our research group: (1) microfluidics engineered PLGA nanoparticles encapsulating cannabidiol (CBD) for radiodermatitis management, (2) inflammation responsive systems incorporating reactive oxygen species (ROS)-cleavable thioketal linkages for selective drug release, and (3) an advanced viscosupplement combining crosslinked hyaluronic acid with curcumin loaded nanoparticles, developed with a pharmaceutical SME for osteoarthritis treatment.

Materials and Methods: PLGA nanoparticles were synthesized using microfluidics to achieve controlled size and efficient CBD encapsulation. Their biological performance was assessed using an artificial skin model of radiation induced injury.

ROS responsive delivery systems were developed by integrating thioketal linkages into polymer backbones, and their physicochemical properties, degradation behavior, and drug release profiles were evaluated under physiological and oxidative conditions.

The viscosupplement was formulated by combining crosslinked hyaluronic acid with curcumin loaded nanoparticles and evaluated in an anterior cruciate ligament transection (ACLT) osteoarthritis model in New Zealand rabbits.

Results: CBD loaded PLGA nanoparticles exhibited high colloidal stability and sustained release. The nanosystem demonstrated antioxidant activity and antibacterial efficacy against Staphylococcus aureus. In experimental radiodermatitis, the

formulation showed radioprotective effects, including increased expression of transglutaminase 1 and laminin 5 after 5–10 Gy irradiation, and enhanced Ki 67 expression after 5 Gy.

Thioketal based ROS responsive polymers selectively degraded in oxidative environments (50–250 μM H_2O_2), enabling controlled, site specific release. These systems also displayed intrinsic antioxidant activity, restoring ROS concentrations to basal levels within 24 h and achieving up to 88.9 ± 2.8% DPPH radical scavenging activity, compared with 42.7 ± 5.8% in controls.

The advanced viscosupplement produced marked chondroprotective effects in vivo. Animals treated with the prepared formulation showed substantially reduced cartilage degradation compared with controls.

Discussion and Conclusion: These three technologies highlight the versatility and translational relevance of polymeric biomaterials. PLGA-CBD nanoparticles show promise for regenerative dermatological applications, while ROS responsive polymers demonstrate how chemical design enables precise, on demand therapeutic release with added antioxidant benefits. The advanced viscosupplement illustrates the potential of combining polymer networks with nanoparticle mediated delivery to enhance osteoarthritis treatment. These systems exemplify how engineered polymeric materials can address diverse unmet needs in regenerative and translational medicine.

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Characterization of Hybrid PLCL Nanofibers Incorporating Stem Cell Derived Secretome: Implications for Regenerative Medicine

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Advancing tissue regeneration requires biomaterials that provide not only structural support but also biologically meaningful cues. In this keynote, I will present our development of hybrid nanofibrous scaffolds composed of poly(L-lactide-co-ε-caprolactone) (PLCL) integrated with bioactive factors derived from Wharton's jelly mesenchymal stem cells (WJ-MSCs), a population residing in the gelatinous connective tissue of the umbilical cord. These scaffolds were fabricated through co-electrospinning into both aligned and random fiber architectures, using an optimized protocol established at the Institute for Bioengineering of Catalonia (IBEC).
We characterized the resulting nanofibers through light microscopy, atomic force microscopy (AFM), and quantitative Fast Fourier Transform (FFT) analysis to assess fiber orientation. We further evaluated the controlled release kinetics of FITC-labeled secretome components and used human adipose-derived MSCs (AD-MSCs) to assess biocompatibility, including cell viability, adhesion, proliferation, and migration.
FFT-based orientation analysis revealed that AD-MSCs cultured on aligned nanofibers exhibited markedly higher anisotropy and directional alignment. Functionally, aligned scaffolds supported robust viability and proliferation and significantly enhanced directed migration. In in vitro artificial wound-closure assays, aligned nanofibers promoted substantially faster healing compared to their randomly oriented counterparts. To begin evaluating their translational potential, we have now advanced these findings into an in vivo setting, initiating preliminary studies in a rat model where the scaffolds are being assessed for biocompatibility and regenerative performance.
Together, these findings highlight the synergistic interplay between nanofiber alignment and biochemical functionalization in shaping cell behavior. They underscore the promise of PLCL-based hybrid nanofibers as next-generation scaffolds for regenerative medicine, particularly in advanced wound healing applications.

Hyaluronan - a simple glycosaminoglycan with multiple functions

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Composed by two altering disaccharide units of D glucuronic acid and N acetyl D glucosamine, hyaluronan (HA) is the simplest glycosaminoglycan in the extracellualr matrix of nearly all tissues. Besides its simplicity, HA has many homeostatic and pathological functions that depend on its molecular weight. High molecular weight (HMW) HA (above 1 MDa) forms entangled, highly hydrated networks that provide viscoelasticity, lubrication, and structural integrity in different tissues and is often used as hydratant and viscosupplement. On the other hand, low molecular weight (LMW) HA obtained during pathological scenrios in which hyaluronidases and oxidative spacies are increased (e.g. injury, chronic inflammatio, tumorogenesis), activates several downstream signalling and act like context-dependent alarm towards cells reprogramming.
Several examples that showcase the importance of the HA molecular weight will be presented. Mechanisms and downstream signalling cascades that are invovled in the recognition and response to HA of different size will be discussed. Main attention will be given to the specific receptors CD44 and RHAMM. The implications in the development of HA-compositions for regenerative purposes will be also debated - approaches that use soluble and immobilised HA and different methodologies for HA immobilisation will be compared. Results obtained with different cells will be shown and discussed in the light of various regenrative scenraios.
The presented data and discussion should provide useful guidelines and considerations for the use of HA in specific clinical cases.
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Therapeutic siRNA-guided differentiation and crosstalk in bone regeneration

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RNA interference mediated by short non-coding RNAs such as siRNAs represents a powerful strategy for transient and catalytic gene regulation in therapeutic applications. In the context of bone tissue engineering, siRNA can enable precise modulation of signaling pathways by selectively silencing inhibitory factors that impair osteogenesis to enhance pro-osteogenic signaling.

Accordingly, we established a microtissue-based platform in which human bone marrow–derived mesenchymal stem cells (hMSCs) are assembled with siRNA-loaded, cross-linked gelatin microparticles to enable localized and sustained gene silencing within the microtissue environment. Based on this concept, we achieved effective silencing of the BMP 2 antagonist Chordin, which resulted in a marked improvement of osteogenic differentiation within microtissues [1].

Effective regeneration depends not only on intrinsic osteogenic responses but also on interactions with surrounding cell populations. In order to investigate the effects of our chordin-silenced microtissues on bone homeostasis, we simulated in vivo conditions in a supplement-free co-culture system of hMSC and human peripheral blood mononuclear cells (hPBMC) [2]. Here, we found increased osteogenic markers in the presence of siRNA treated microtissues, such as Osteoprotegerin and alkaline phosphatase activity, while markers of osteoclast differentiation remained unchanged indicating osteoanabolic effects [2].

In addition, bone is a highly vascularized tissue whose successful regeneration requires both osteogenic and angiogenic processes. To address this highly important interaction, we established a co-culture model composed of osteogenic and vascular microtissues embedded in a fibrin hydrogel to investigate siRNA effects on microtissue interaction [3]. After separate pre-differentiation, both microtissue types were co-cultured in a fibrin hydrogel for up to 5 weeks. We found that Chordin siRNA enhanced crosstalk with vascularizing microtissues, resulting in improved sprouting and, conversely, enhanced osteogenic differentiation [3].

In conclusion, we set up a microtissue based co-culture system able to indicate siRNA effects on the osteogenic-vascular crosstalk. Our work may pave the way for microtissues based bottom-up tissue engineering approaches supported by therapeutic small non-coding RNAs.

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Biomaterials with distinct levels of cells contents

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Materials are ubiquitous in Tissue Engineering (TE) solutions, as a structural support for adherent cells and as a vehicle to provide relevant biochemical and biophysical signals to control cell behavior. Different types of natural-based macromolecular materials have been proposed to prepare scaffolds for TE, including porous structures, hydrogels or microparticles. Those can be used as acellular structures, with the capability to elicit favorable biological reactions upon implantation, towards tissue repair. We have been proposing the use of human-derived proteins that, upon chemical modification, could be used to generate adequate three-dimensional microenvironments to interact adequately with cells, that could be integrated with distinct densities. We have selected two sources of such materials: (i) platelet lysates, containing mostly globular proteins including relevant growth factors with highly regenerative potential; and (ii) proteins from amniotic membrane and placenta, composed of fibrillar proteins such as collagens and other components of the extra-cellular matrix. Due to their hydrophilic nature and richness in chemically active groups, these proteins can be chemical modified to generate materials with new or improved properties, while maintaining the biochemical features of human tissues.
In an extreme situation, we have been also leveraging the important role of the cells in the development of constructs for TE. In our group we have been proposing possibilities of using lower relative amount of biomaterials in the hybrid constructs in order to assemble human cells in different geometries, including partially coated cells, spherical aggregates (spheroids), fibres (fiberoids), membranes (cell-sheets) and hydrogel-like materials (cellgels). Examples will be given on how bioengineered constructs could be obtained at different dimensional and length scales, mainly focusing on bone tissue regeneration.

Competence Center "Leonardo da Vinci": A Platform for Regenerative Medicine, Innovation, and Technology Transfer

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The Competence Center "Leonardo da Vinci" at Medical University – Pleven (MU-Pleven) represents one of the most ambitious research infrastructure investments in Bulgarian higher education. Established in 2018 through EU co-financing under the Operational Programme "Science and Education for Intelligent Growth" (Project BG05M2OP001-1.002-0010-C01, Phase 1 budget: 23.7 million BGN), and currently undergoing expansion through a second phase funded by the Programme "Scientific Research, Innovation and Digitalization for Smart Transformation" (Project BG16RFPR002-1.014-0002, Phase 2 budget: 14+ million BGN), the Center serves as a multidisciplinary platform for personalized medicine, 3D and telemedicine technologies, and robotic-assisted and minimally invasive surgery.

This presentation outlines the Center's strategic vision, infrastructure, key achievements, scientific output, and its evolving role as a platform for regenerative medicine, innovation, and technology transfer within the European research landscape.

Background and Objectives: Medical University – Pleven is a pioneer in robotic surgery, telemedicine, 3D medicine, bioprinting, and the integration of advanced technologies in education and clinical practice. The Center was conceived to address a critical gap in Southeastern European research infrastructure by creating a world-class facility that bridges fundamental research and clinical application. The consortium includes three institutions: MU-Pleven (lead partner, hosting 7 laboratories), Medical University "Prof. Dr. Paraskev Stoyanov" – Varna (Center for Robotic Surgery with Da Vinci Xi system), and the Institute of Robotics at the Bulgarian Academy of Sciences (2 robotics research laboratories).

The research program is organized into four work packages: (1) Personalized Medicine – precision oncology, genomic medicine, and precision pathology with telepathology; (2) 3D and Telemedicine – 3D printing, bioprinting, virtual reality surgical training, and telesurgery navigation; (3) Minimally Invasive Surgery – stereotactic biopsies and integrated interdisciplinary operating rooms; and (4) Robotic-Assisted Surgery – utilizing the Da Vinci Xi system with four specialized surgical teams in oncogynecology, urology, and general surgery.

Infrastructure and Laboratories: The Center comprises 10 laboratories equipped with high-technology apparatus and specialized software. At MU-Pleven, seven laboratories are operational: Laboratory for Precision Oncology and Genomic Medicine; Laboratory

for Precision Pathology with Application of Telepathology, Morphometry and Telemedicine Methods; Laboratory for 3D Printing, Modeling and Analysis; Laboratory for Research and Training of Surgeons in a Virtual Reality (VR) Environment; Integrated Interdisciplinary Operating Room with Navigation and Telesurgery Systems; Laboratory for Stereotactic Vacuum Aspiration Biopsies; and the Center for Robotic-Assisted Surgery. At MU-Varna, a Center for Robotic Surgery was established with a purchased Da Vinci Xi robotic system of the latest generation, complete with a training simulator and installation kit. The Institute of Robotics at BAS operates two additional laboratories dedicated to robotics research and AI applications in medicine.

Key Results and Achievements (Phase 1: 2018–2023): During the Phase 1 implementation period, the Center achieved significant milestones across multiple dimensions. A total of 114 new researchers were appointed, including 40 young scientists under the age of 34, contributing to the formation of a robust and dynamic research workforce. The Center supported 20 doctoral students, postdoctoral researchers, and specialists, with 8 PhD dissertations successfully defended.

Scientific output has been substantial: approximately 60 publications appeared in prestigious national, European, and international medical journals, with a cumulative impact factor of 74.107. Among the notable publications is a landmark case report in the European Journal of Medical Research (2023) describing the first application of Da Vinci robotic surgery combined with 3D printing technology in septal myectomy for hypertrophic obstructive cardiomyopathy (HOCM), utilizing a patient-specific 1:1 scale 3D-printed heart model for preoperative planning. A foundational paper on the Center's establishment was published in the European Journal of Public Health (Vol. 29, Suppl. 4, 2019).

In terms of intellectual property, 8 patent applications have been submitted with 2 approved. In a landmark development in 2025–2026, MU-Pleven filed its first international patent applications in the United Kingdom and signed a Memorandum of Cooperation with the Patent Office of the Republic of Bulgaria, establishing a foundation for long-term partnership in industrial property protection. Additionally, 43 contracts for joint research projects were signed with industry and academic partners, and over 95% of the total Phase 1 budget was utilized.

Innovation and Technology Transfer: The Center is actively building an innovation ecosystem that extends beyond academic research. With the second phase of EU funding (BG16RFPR002-1.014-0002, budget exceeding 14 million BGN), the focus is on expanding robotic surgery systems and capabilities, advancing 3D technologies and genetic sequencing, developing telemedicine solutions, and strengthening the technology transfer pipeline from laboratory to clinical practice.

MU-Pleven's unique position as the only Bulgarian university integrating human medicine, veterinary medicine, and pharmacy creates strong foundations for

interdisciplinary research, particularly in regenerative medicine, where convergences between 3D bioprinting, stem cell research, AI-driven personalized treatment, and advanced genetic sequencing open new frontiers for translational science.

Conclusions: The Competence Center "Leonardo da Vinci" demonstrates how strategic EU investment, combined with institutional vision and cross-institutional partnership, can transform regional research capacity. With its comprehensive infrastructure, growing scientific output, first international patents, and expanding industry collaborations, the Center is positioned as a leading platform for regenerative medicine, innovation, and technology transfer in Southeastern Europe.

Keywords: competence center, personalized medicine, robotic surgery, 3D printing, telemedicine, regenerative medicine, technology transfer, Da Vinci Xi, EU funding, Medical University Pleven

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Mechanochemical information in cells and Emergent properties in multicellular organisms.

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In my biomedical engineering research, from the start to now, I had to use pieces, parts, cells, molecules of the human body. As many scientists in the field.
One question that stayed in my mind until now is: how the properties, functional movements and interactions of the parts relate to the similar qualities of the whole.
It seems that this is an omnipresent question in all scientific fields, not only in biology or physics but in societal sciences as well.
In this presentation I will attempt to use the information (messages) that operates within a cell and further in the multicellular organism as a paradigm to explore what is known as emergency, that is the emergency of new properties of the whole that cannot be predicted from the known properties of the parts.
A literature review is used. Not only recent one, but, but looking further back, it seems that what emerges is the powerful method of dialectics as a useful approach towards understanding the natural workings of life.

Translating Tendon Biology into Regenerative Therapies

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Tendons are matrix-dominated tissues capable of withstanding substantial tensile forces; nevertheless, injuries can occur even following low-energy insults. Tendinopathies represent a major clinical burden, accounting for approximately 30–50% of musculoskeletal-related primary care visits worldwide. These conditions are characterized by pain, swelling, and restricted range of motion, affecting individuals of all ages during both occupational and recreational activities. Furthermore, such patients are predisposed to tendon rupture and extended healing phases that can be both burdensome and slow. In the European Union alone, tendinopathies generate an estimated €800 million in annual healthcare costs.
Despite significant advances in our understanding of tendon structure, cell biology, biomechanical environments, and cell–biomaterial interactions for therapeutic applications, research in tendon biology and pathology remains fragmented.
In this talk, I will first address the socioeconomic burden of tendinopathy and its end-stage manifestation, tendon rupture. I will then provide an overview of the current understanding of tendinopathy pathogenesis, highlighting the key cellular and molecular players involved. Finally, I will discuss the evolution of tendinopathy management strategies and present insights from our basic and preclinical research that may contribute to the development of novel regenerative approaches.

3D bioprinting – high hopes for tissue repair

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The innovative 3D bioprinting technology is based on combining living cells, growth and nutritional factors, and biomaterials to create spatially organized tissues and organs with a structure and function mimicking those of normal ones. It serves as a single instrument, following a single algorithm but allowing for multiple applications. The ideal vitro 3D model includes several cell types, provides an interactive 3D microenvironment, models cell behavior and function, and enables the growth of blood and lymph vessels. The organ-on-a-chip models are established as multi-channel 3D microfluidic cell cultures that simulate the function, mechanics, and physiological response of an entire organ or system. These advanced technologies have multiple biomedical applications in tissue engineering and organ transplantations, in managing congenital heart anomalies, bone and cartilage defects, skin lesions, and wound healing. They are a precious tool in personalized oncology, serve as platforms for drug screening and drug delivery systems. There are also promising results in endocrinology, nephrology, rheumatology including our personal experience in cartilage and bone repair. The challenges 3D bioprinting has not overcome yet are the proper vascularization and innervation of tissues and organs, the generation of organs capable of growing together with the pediatric patient's body, and the development of self-growing and biodegradable polymer materials. Despite some pitfalls and time-consuming improvement of current appliances and methodology, 3D bioprinting offers high hope for tissue repair opening new horizons for regenerative and translational medicine.

Oral Contributions

Innovative Biomaterials and Emerging Biotechnologies in Wound Healing: Insights from a Surgeon

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Background: Chronic and complex wounds remain a significant surgical challenge, affecting millions worldwide and generating substantial healthcare burden. Despite advances in conventional wound management, many wounds fail to respond adequately due to impaired vascularization, persistent inflammation, or extensive tissue loss. Recent breakthroughs in biomaterials science and regenerative biotechnology offer promising avenues for improving healing outcomes. This abstract synthesizes current evidence on four major technological domains—advanced scaffolds, growth-factor and cell-based therapies, 3D bioprinting, and nanofiber drug-delivery systems—from the perspective of their clinical relevance and translational potential.
Materials and Methods: This structured review integrates data from recent clinical trials, translational studies, and technological assessments published between 2019 and 2025. Topics include collagen and decellularized extracellular matrix scaffolds, electrospun nanofibers, smart hydrogels, platelet-rich plasma (PRP), mesenchymal stem cells (MSCs), exosome therapeutics, in-situ and multi-cellular bioprinting, and stimuli-responsive nanofiber delivery platforms. Evidence was synthesized with emphasis on clinical efficacy, mechanisms of action, and feasibility for surgical practice.
Results: Decellularized extracellular matrix scaffolds demonstrated 20–50% faster re-epithelialization and reduced scarring compared with standard collagen dressings. PRP shortened healing time by approximately one week in chronic wounds, while MSC-based therapies showed up to 10-fold acceleration of wound closure in early trials. Exosome-based treatments, particularly Wharton's jelly–derived MSC exosomes, produced superior healing rates in randomized controlled studies. Advances in 3D bioprinting enabled fabrication of autologous skin layers in situ and multi-cellular constructs integrating keratinocytes, fibroblasts, melanocytes, and endothelial cells with successful in vivo incorporation. Smart nanofiber systems provided controlled, on-demand delivery of antimicrobials, antioxidants, or growth factors in response to pH, ROS, temperature, or glucose levels, enhancing precision and reducing systemic exposure.

Discussion and Conclusion: Emerging biomaterials and biotechnologies are reshaping wound care by enabling personalized, biologically informed, and multifunctional solutions. From a surgical perspective, their successful translation requires standardized manufacturing, cost-effectiveness, robust clinical trials, and workflow-compatible application methods. Integration of scaffolds, cellular therapies, bioprinting, and smart drug delivery is expected to produce next-generation multimodal systems capable of transforming outcomes in chronic and complex wounds. Continued collaboration between surgeons, biomaterials scientists, and bioengineers will be essential for achieving widespread clinical adoption.

Paracrine effects of buccal fat pad–derived dedifferentiated fat cells on bone and cartilage regeneration

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The repair of significant bone loss resulting from trauma, tumor resection, or radiotherapy remains a critical challenge in maxillofacial surgery. While traditional reconstructive methods—such as autologous bone grafting and osteosynthesis—are the clinical standard, they are often limited by donor site morbidity and inadequate tissue integration. In this context, stem cell-based therapies have emerged as a promising adjunctive approach to enhance the biological regenerative capacity and improve healing outcomes.

Recently, research focus has shifted from the stem cells themselves to the key role of their secretome in driving tissue repair. This study focuses on dedifferentiated fat cells (DFATs) isolated from the Buccal Fat Pad (BFP), which share similar multilineage differentiation properties with stem cells, making them an excellent model for regenerative studies. The BFP serves as an ideal, easily accessible autologous source for cell isolation during routine oral and maxillofacial procedures, eliminating the need for invasive harvesting from remote donor sites.

Our research explores the paracrine effects of the BFP-derived DFAT cell secretome on specific target cells involved in bone metabolism and remodeling: osteoblasts, mesenchymal stem cells (MSCs), and endothelial cells. Following the isolation and characterization of BFP-derived cells via flow cytometry, conditioned media was collected to analyze its biological impact. To identify the underlying molecular mechanisms, multiplex protein analysis will also be conducted to profile the regenerative cytokines and growth factors within the secretome.

While this work is ongoing, preliminary results indicate that the DFAT secretome significantly increases the proliferation of both pooled MSCs and human periosteum-derived cells (hPC), as measured by Alamar Blue assays. These early trends suggest that the BFP-derived secretome possesses mitogenic properties that could enhance progenitor cell recruitment at injury sites.

A Translational Framework for Regeneration of Inferior Turbinate Erectile Tissue Using Injectable 3D Macroporous Hydrogel Scaffolds

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Background: Empty Nose Syndrome (ENS) and related iatrogenic nasal cavity dysfunction following turbinate surgery result from loss of a functional nasal organ rather than simple volume depletion. Current evidence indicates that ENS involves altered airflow dynamics, reduced mucosal area, impaired humidification, chronic inflammation, diminished sensory function, and neural injury. Existing augmentation strategies such as platelet-rich plasma, stromal vascular fraction, and autologous fat grafting can improve symptoms and mucosal healing, but they do not reliably reconstruct the specialized functional architecture of the inferior turbinate.
Objective: To propose a translational framework for regenerating inferior turbinate functional soft tissue using injectable macroporous hydrogel scaffolds.
Conceptual approach: Injectable macroporous hydrogels assembled from preformed microgels provide interconnected pores that support cell infiltration, cell spreading, oxygen and nutrient transport, and potential vascular patterning. Two regenerative strategies are considered: (1) pre-seeding the scaffold with regenerative and/or endothelial-supportive cells before gelation, and (2) implanting a cell-free scaffold designed for host-cell recruitment and remodeling. The scaffold is intended to serve as a biodegradable structural template, enabling vascularization, mucosal restoration, and later neurofunctional integration.
Rationale: Clinical ENS studies show that fat grafting with adipose-derived stem cells improves symptom scores, mucociliary clearance, mucosal histology, and markers of epithelial restoration, but outcomes remain partial and structurally uncontrolled. A macroporous injectable scaffold may address this limitation by coupling regenerative biology with architectural guidance.
Conclusion: Injectable macroporous hydrogel scaffolds represent a plausible next-generation platform for inferior turbinate regeneration. By moving from bulk augmentation toward guided tissue reconstruction, this approach could form the basis for future preclinical development aimed at restoring physiological nasal function in ENS patients suffering from iatrogenic nasal disfunction.

Biomimetic Microgels in Tissue Regeneration and Disease Models.

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Background: A microgel consists of a dispersion of microparticles in an aqueous medium. When used as a 3D environment in an in vitro disease model, cells are seeded between the microspheres and the culture is carried out under static or dynamic conditions. When in vivo tissue regeneration, the agglomerate of cells and microspheres can be injected into the site of damage. In either case, the environment encountered by the cells is analogous to that which they would encounter if encapsulated in a hydrogel or seeded into the pores of a scaffold, with the essential difference that, during culture or the regeneration process, the cells have mobility and can accommodate the environment to house the extracellular matrix they themselves produce or spatially organise the newly formed tissue.

Materials and Methods: This paper presents microgels produced by microfluidics or emulsion that have been made biomimetic by grafting biomolecules characteristic of the tissue to be simulated onto the surface of the microspheres that form them: proteins such as collagen, gelatin, fibronectin or laminin, and polysaccharides such as hyaluronic acid, chondroitin sulphate, heparan sulphate, heparin, chitosan and others.

Results and discussion: These microspheres have been used in the regeneration of articular cartilage in rabbit knee and minipig knee models. It is shown how, during the growth of new tissue, the microspheres are displaced towards the subchondral bone, leaving space for the newly formed cartilage to acquire the spatial configuration characteristic of hyaline cartilage. In a model of multiple myeloma disease, co-cultures of tumour cells and mesenchymal stem cells have been performed in microgels that present the biomolecules of the bone marrow that are important for the indirect interaction between the two cell types and, in general, for tumour progression, observing how, in this environment, tumour cells develop resistance to drugs, making the model more predictive for the development of new drugs than conventional 2D or suspension systems. In solid environment models such as lung cancer, it has been shown how cells are capable of forming organoids that collect cells and microspheres inside them. Something similar occurs in hepatocytes from cell lines used in a liver toxicity model when they are cultured in microspheres produced from decellularized liver tissue.

Uncovering the Biological Properties of Dental-Derived Mesenchymal Stem Cells

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Background: The objective of the present study is to assess the multilineage differentiation capacity of mesenchymal stem cells of dental origin. Dental tissues are proven to harbor a number of non-differentiated mesenchymal stem cells. The present work aims to compare the different characteristics of six types of dental stem cells derived from the oral cavity: dental pulp stem cells (DPSC), stem cells from human exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSC), stem cells from the apical papilla (SCAP), bone marrow mesenchymal stem cells (BMSC), and gingival mesenchymal stem cells (GMSC). We characterized them and assessed their capacity for multilineage differentiation.
Materials and Methods: Mesenchymal cells were isolated and expanded in vitro. Cells were grown up to 3 passages. Using immunofluorescence and RT-PCR techniques, we analyzed the cells for stem cell, differentiation, adhesion, and extracellular matrix markers; the ability to proliferate in vitro; and multilineage differentiation potential.
Results: After 2-4 weeks of differentiation all cultures were positively stained for Ca2+ aggregates with Alizarin red proving osteogenic differentiation. The Oil Red O staining revealed number of fatty droplets in the cytoplasm of the adipogenically differentiated cells. All cultures proved to be able for chondrogenic differentiation: alcian blue staining showed production of cartilage specific proteoglycans. Epithelial markers CK10 and P63 were positive after epithelial induction. For hepatic differentiation, DPSC and SHED cells demonstrated significant number of cells positive for alpha-fetoprotein, albumin, hepatic nuclear factor 4alpha, insulin-like growth factor 1 and CPS-1 after hepatic differentiation. The concentration of urea in the media increased. Moreover, glycogen was found in the cells' cytoplasm. After the pancreatic differentiation, in DPSC and SHED the expression of endocrine markers insulin, glucagon, somatostatin and pancreatic polypeptide, GLUT2, and the exocrine marker pancreatic amylase were found positive by immunocytochemistry and flow-cytometry. Real time RT-PCR revealed the expression of pancreatically specific transcription factors.
Discussion and Conclusion: The dental mesenchymal cell cultures acquired morphological and functional characteristics of osteoblasts, adipocytes, chondrocytes, hepatocytes, pancreatic and epithelial cells. Multilineage differentiation of mesenchymal stem cells dental origin can bring in vitro cell differentiation methods closer to clinics.

Mesenchymal Stem Cell Interactions with Glycated Collagen: Adhesion Dynamics, Mechanotransduction, and Matrix Remodeling

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Mesenchymal stem cells (MSCs) are pivotal mediators of tissue repair and extracellular matrix (ECM) remodeling, relying on collagen as a structural scaffold. Non-enzymatic glycation of collagen, a hallmark of diabetes and aging, profoundly disrupts MSC–matrix interactions. Using human adipose tissue-derived MSCs (ADMSCs) and in vitro glycated rat tail collagen (GL1: 1-day; GL5: 5-day, 0.5 M glucose), this study characterizes how glycation alters collagen biophysics and MSC behavior across morphological, biomechanical, and mechanotransductive dimensions.

Atomic force microscopy (AFM) revealed progressive changes in collagen surface properties: surface potential declined from ≈789 mV (native) to ≈559 mV in GL1; surface roughness increased from 3.0 ± 0.4 nm to 7.70 ± 0.6 nm in GL5; and Young's modulus dropped from 34.8 ± 5.4 MPa to 6.90 ± 0.5 MPa (GL1) and 2.07 ± 0.3 MPa (GL5). GL5 showed partial fibrillar restoration relative to disordered GL1 networks. FTIR spectroscopy and differential scanning calorimetry confirmed subtle structural and thermodynamic changes. MSC morphometry showed reductions in cell spreading area from 246.8 μm² (native) to 216.8 μm² (GL1) and 163.7 μm² (GL5), with parallel perimeter decreases from 112.9 μm to 95.1 and 86.2 μm, reflecting impaired integrin recognition and focal adhesion maturation (static conditions). Adhesion followed a biphasic pattern: enhanced attachment within the first 30 minutes, then progressive decline over two hours. Under dynamic flow (BioFlux microfluidic system), MSCs adhered within 3–5 minutes, far faster than the classical 2-hour static protocol, yet displayed weaker adhesion under shear stress (1–20 dyn/cm²) than on native collagen. A dual-receptor mechanism was identified: an early phase mediated by the receptor for advanced glycation end-products (RAGE), active within the first 30 minutes, followed by an integrin-dependent phase governing stable adhesion. YAP/TAZ nuclear localization, a key mechano-transduction indicator, peaked during RAGE engagement and was

progressively attenuated as integrin-based focal adhesions matured, demonstrating dynamic coupling between receptor usage and mechanosensitive signaling. Collagen remodeling was also impaired, but endogenous collagen synthesis remained constitutively active at all time points (30 min, 2 h, 5 h), indicating preserved biosynthetic capacity.

These findings establish that glycation reshapes MSC adhesion kinetics, mechanosensitive signaling, and matrix remodeling through a dual RAGE/integrin mechanism, with implications for regenerative strategies targeting diabetic wounds and aged tissues.

Divergent Mitochondrial Responses to Palmitate-induced Lipotoxic Stress: Image-Based Analysis of Network Dynamics and Membrane Potential in Two Main Adipose Tissue-Derived Cells

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Background: Elevated circulating free fatty acids, such as palmitate, induce lipotoxicity in adipose tissue, contributing to mitochondrial dysfunction and metabolic disorders. Human adipocytes and adipose-derived mesenchymal stem cells (hAdMSCs) represent two key cell types in adipose tissue with distinct roles in lipid storage and tissue homeostasis, yet their differential responses to lipotoxic stress remain poorly understood.
Materials and Methods: Primary hAdMSCs and differentiated adipocytes were treated with different concentrations of sodium palmitate (SP) for 24 hours. Mitochondrial network dynamics were assessed by live-cell imaging with MitoBright LT Green, followed by automated segmentation and quantification of key network parameters using python-based software Napari, plugin Nellie, and custom Python analysis pipelines. Membrane potential was evaluated with JC-1 dye (ratiometric analysis), and mitophagy with Mitophagy Kit.
Results: In adipocytes, 250 μM SP induced dynamic network remodeling with transient elongation and volume increase peaking around 12–18 hours (suggestive of hyperfusion), followed by fragmentation and partial recovery by 24 hours. In contrast, hAdMSCs exhibited gradual, linear reduction in branch length, total branch number, tortuosity, and mitochondrial volume across 24 hours without clear peaks. Following 24 hours treatment, in both cell types 500 μM SP caused a less pronounced decline in network parameters compared to 250 μM SP, suggesting a non-linear dose-response curve to palmitate. Interestingly, while palmitate induced a dose-dependent decrease in mitochondrial membrane potential (DeltaPsim) in mature adipocytes, hAdMSCs exhibited the opposite response: a significant increase in DeltaPsim (hyperpolarization) at both 250 μM and 500 μM palmitate concentrations. This paradoxical hyperpolarization in precursor cells, combined with pronounced mitochondrial fragmentation, suggests a maladaptive stress response. Mitophagy analysis data indicated increased autophagic clearance under high-dose SP, particularly in adipocytes.

Discussion and Conclusion: Adipocytes display a reversible, biphasic mitochondrial response to moderate lipotoxicity (transient hyperfusion followed by fragmentation), whereas hAdMSCs exhibit progressive network simplification but preserved membrane potential, likely reflecting stem-cell adaptive mechanisms such as enhanced beta-oxidation and mild uncoupling. However, this maladaptive state is prone to excessive ROS production via reverse electron transport and accelerated damage. These divergent responses highlight cell-type-specific resilience in adipose tissue under fatty acid overload, with implications for obesity-related mitochondrial pathology and therapeutic targeting of stem-cell populations.

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Multimodality Therapeutic Approach in Burn Treatment: The Role of PRGF, Photobiomodulation, and Cold Atmospheric Plasma.

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Introduction: Burn injuries represent a significant global health burden, often complicated by infection, delayed healing, and scarring. Conventional management includes debridement, antimicrobial therapy, and grafting; however, emerging regenerative and biophysical therapies aim to enhance tissue repair. Plasma Rich in Growth Factors (PRGF), photobiomodulation (PBM), and cold atmospheric plasma (CAP) have gained attention due to their regenerative, anti-inflammatory, and antimicrobial properties. This study presents the efficacy of these modalities in burn treatment showing an example based on a patient.
Methods: A patient with severe burns 70% skin surface, grade IIb was treated with the three modalities.
Results: PRGF promotes wound healing through the controlled release of growth factors such as platelet-derived growth factor (PDGF) and transforming growth factor-β (TGF-β), enhancing angiogenesis and epithelialization. PBM has demonstrated significant efficacy in accelerating burn wound healing by activating endogenous TGF-β1 signaling, reducing inflammation, and improving cellular proliferation and tissue remodeling. CAP exhibits potent antimicrobial effects, effectively reducing bacterial load without impairing host tissue regeneration, addressing a major limitation of conventional antiseptics. Additionally, CAP has been shown to enhance wound closure, increase dermal and epidermal regeneration, and upregulate growth factors such as TGF-β1 and connective tissue growth factor (CTGF) . Combined, these therapies contribute to improved healing kinetics, reduced infection rates, and enhanced tissue quality as will be shown in the patient's example. In the presented patient the multimodality treatment led to complete resolution of the signs of burning, preventing from fibrosis.
Conclusion: PRGF, photobiomodulation, and cold atmospheric plasma represent promising adjunctive therapies in burn management. Their synergistic effects combining regenerative stimulation, anti-inflammatory modulation, and antimicrobial activity offer significant advantages over traditional treatments. Further large-scale clinical trials are required to standardize protocols and confirm long-term efficacy and safety.

Regeneration of critical bone defects using bioprinted MSCs in a mouse model

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Critical-sized bone defects represent a significant challenge in orthopedic surgery, as they will not heal spontaneously and often require complex reconstruction. Current gold-standard treatments, such as autologous bone grafting, are limited by donor site morbidity and insufficient graft availability, underscoring the need for alternative regenerative strategies.

Mesenchymal stem cells (MSCs) have emerged as a key cell source for bone tissue engineering due to their osteogenic differentiation potential and robust paracrine activity. Through the secretion of bioactive factors, MSCs modulate the local immune response, promote angiogenesis, and recruit host cells to the injury site, thereby stimulating endogenous repair mechanisms.

Bioprinting offers distinct advantages over conventional scaffold fabrication by enabling the precise, spatially controlled deposition of cells, growth factors, and biomaterials. This technology allows for the creation of patient-specific constructs that closely mimic the complex architecture of native bone tissue.

The convergence of bioprinting with MSC biology holds significant promise for clinical bone regeneration. Current research focuses on optimizing bioink formulations to create a supportive niche that directs MSC fate toward osteogenesis while maintaining high cell viability during and after the printing process.

Four types of bioprinted constructs were prepared using two commercial bioinks (CELLINK BONE and GelXA BONE), with and without embedded MSCs. These were implanted in a critical-sized cranial defect mouse model and compared to empty defects (negative control). Bone regeneration was assessed using micro-computed tomography (micro-CT) and new bone formation was confirmed by histology.

After 6 weeks, micro-CT analysis revealed that the addition of MSCs to CELLINK BONE bioink significantly enhanced bone regeneration compared to CELLINK BONE alone. While a similar trend was observed in the GelXA BONE group, the difference did not reach statistical significance ($p > 0.05$). Defects treated with acellular bioinks (CELLINK

BONE or GelXA BONE alone) did not show significant regeneration compared to empty control defects.

These findings underscore the critical role of MSCs in mediating bone regeneration within bioprinted constructs. The superior performance of MSCs in the CELLINK BONE group compared to GelXA BONE highlights that the biochemical and mechanical properties of commercial bioinks can significantly influence osteogenic outcomes. Further investigation is required to determine whether this effect translates to other bone defect models and to elucidate the specific bioink characteristics driving MSC-mediated repair.

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Regenerative Strategies for Alopecia Using Platelet-Derived Exosomes

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Background: Alopecia is a common dermatological condition with a multifactorial aetiology. Conventional therapies, such as Minoxidil, Finasteride, and Spironolactone, require long-term use and may cause adverse effects, highlighting the need for novel regenerative approaches. Platelet-derived exosomes (PDE) have emerged as a promising cell-free therapeutic option. These vesicles are rich in growth factors and signaling molecules that activate stem cells in the hair follicle, modulate the Wnt/β-catenin pathway, and prolong the anagen phase, thereby promoting hair growth. Their autologous origin reduces immunogenicity, and their stability supports clinical use.
Materials and Methods: The study cohort included 20 male patients with alopecia treated with topical Minoxidil and 7 female patients treated with Spironolactone (100 mg/day) who showed a suboptimal response. The control group consisted of 10 male and 3 female patients with untreated alopecia.
Venous blood samples were collected in sodium citrate vacuum tubes and processed within 2 hours. Platelets were isolated by differential centrifugation at 22°C and resuspended in phosphate-buffered saline (PBS). Exosome release was induced by platelet activation using a 10% $CaCl_2$ solution. Samples then underwent sequential centrifugation at increasing speeds at 22°C to remove residual cells and larger vesicles. The exosomal fraction was isolated by ultracentrifugation at 4°C. The final pellet was resuspended in PBS and stored at −80°C.
Exosome identification was performed using PKH26 fluorescent labelling, allowing visualisation as discrete red fluorescent particles under a Leica THUNDER microscope.
Results: Fluorescence microscopy of PKH26-labelled samples showed numerous discrete red fluorescent signals consistent with exosomes. The uniform distribution and lack of significant aggregation suggest effective isolation and purification, as well as good structural stability.
These findings support further application of PDE in the study cohort. The exosomes were administered through topical application by rubbing onto affected scalp areas. Clinical follow-up will include both quantitative and qualitative assessment of density and reduction in hair shedding.
Discussion: The results demonstrate that PDE can be isolated with sufficient purity and stability for therapeutic use. However, further validation by Western blot analysis with

established specific exosomal and platelet markers. Topical dermal administration is a minimally invasive, clinically practical delivery method that allows direct interaction with the hair follicle environment, promotes stem cell activation, and regulates key pathways involved in the hair growth cycle. The autologous nature of the exosomes reduces immunological risk and supports personalised therapy. Expected therapeutic outcomes include reduced hair loss and increased hair density in patients who have a poor response to standard treatments such as Minoxidil and Spironolactone.

PDE represents a promising cell-free regenerative approach for treating alopecia. Their favourable safety profile, due to their autologous origin, along with their stability, storage potential, and suitability for topical application, highlights their clinical promise. However, a larger cohort and a longer time are needed to confirm their effectiveness.

Material Design Strategies for Advanced Biofabrication

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Background: Precision bioprinting depends not only on the printing platform, but critically on the design of the material system itself, including bioinks, photocurable resins, and embedding media for embedded extrusion bioprinting. Each printing modality imposes distinct requirements on viscosity, yield stress, crosslinking kinetics, interfacial stability, and cytocompatibility. Rational formulation of these material systems is therefore essential for achieving high printing fidelity, structural stability, and biological relevance in advanced biofabrication.
Materials and Methods: A precision biofabrication framework was developed using embedded extrusion and resinbased printing. For embedded extrusion printing, particular attention was given to the interaction between the ink and the support bath, gelatin-based hydrogel microparticles, including support rheology, reversibility of support removal, and cell compatibility throughout the full biofabrication process. Thus, material formulations were optimized for low-viscosity alginate, collagen-based systems at both acidic and neutral pH, and GelMA (gelatin methacryloyl) inks. For resin-based bioprinting, GelMA formulations were evaluated with respect to viscosity, photoreactivity, resolution, and process compatibility with live cells.
Results: In embedded extrusion bioprinting, the proprietary support medium enabled printing both in-plane and out-of-plane at arbitrary angles, with fibre diameters down to 200 μm, primarily determined by the nozzle diameter, while maintaining high print fidelity. Optimized construct recovery conditions were conducive to high post-print cell viability. In parallel, resin-based systems enabled the fabrication of features smaller than 50 μm and channels narrower than 500 μm, resolutions that are impossible to achieve with other bioprinting modalities. The use of blue light for photocuring did not compromise cell viability, even at high exposure doses. In contrast, radical-driven photopolymerization was the major source of cytotoxicity in the presence of living cells. Overall, the most effective strategies relied on understanding and tailoring the complete material environment rather than optimizing only the printable phase.
Discussion and Conclusion: Advanced biofabrication requires a shift from printer-centered to material-centered design. Bioinks, resins, and embedding media are not passive carriers, but active determinants of resolution, reproducibility, and biological performance. Rational formulation of these materials enables greater precision and broadens the design space for complex tissue constructs. This perspective supports the

development of next-generation material systems for regenerative and translational medicine.

3D-printed bioreactor as a model system for artificial cartilage tissue

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The construction of successful artificial organs requires the recreation of in vivo condition in vitro. Part of the limitation of 2D cell cultures is that the cells forgot how to communicate on 3D scale. Therefore, application of bioreactors, mimicking the biophysical conditions in vitro is essential to overcome this problem. Cartilage, due to its specific architecture is a good candidate for a tissue engineering, especially because it lacks blood vessels, but also because it has diminished regeneration capabilities. For construction of our cartilage bioreactor, we used 3D-printer and thermo stabile, transparent polycarbonate ink (Ultimaker S5, UltiMaker, Netherlands), which allows for rapid development and correction of the designed models. Initially we started with three different concept designs aiming on sterility and accessibility of the system that will closely resemble knee joint movement. After in-depth comparison of our three prototypes, we selected and produced a full size model of the best concept. The selected model is easy to handle, allows for stimulation of two different cartilage constructs and represent a close system with minimum risk of contamination. In parallel to the bioreactor design, we developed a motor system, which simulate the joint movement. The system use a step motor engine that can move the cartilage construct with variable speed and to a desire angle. Furthermore, due to the unique application of the culture media, the constructs will experience a combination of mechanical stimulation and fluid friction that will further increase the compression onto the cartilage construct. In conclusion, we believe that our cartilage bioreactor present a good system for development and studying of cartilage constructs that will resemble the in vivo cartilage tissue. Thus, it will allow for production of efficient artificial cartilage construct that can replace a used up cartilage tissue in joints.

IL-8 as a marker for early in vitro education of human bone marrow mesenchymal stem cells by multiple myeloma cell lines

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Background: Multiple myeloma (MM) is a hematologic malignancy characterized by the clonal expansion of neoplastic plasma cells in the bone marrow (BM), where tumor progression strongly depends on microenvironment interactions. In MM patients, MSCs acquire a myeloma-educated phenotype with a tumor-supportive secretory profile. This phenomenon could allow the use of secretome from educated MSCs as a simpler alternative to MSC-MM co-culture. However, MSCs from healthy donors do not always display a tumor-supportive phenotype, making in vitro modeling difficult. Healthy MSCs can be educated in vitro to produce a protumoral secretome by adding inductors, such as MM cell lines. While most studies analyze transcriptional changes after short (24-48 h) MM exposure, in vivo education occurs over longer periods. We therefore examined whether 72 h exposure to MM cell lines could induce early transcriptional traits associated with MSC education that could reproduce a protumoral secretome.
Materials and Methods: Human BM MSCs (Promocell, passage 5) were exposed to different MM cell lines (RPMI8226, U266, or MM1.S) using (i) 50% v/v MM secretome, (ii) transwell co-culture (0.4 μm inserts; 10:1 MM:MSC), or (iii) direct co-culture (10:1). After 72 h, MM stimuli were removed; one third of samples were collected immediately (0 h), and the rest cultured for 48 or 96 h. In direct co-culture, MM cells were depleted with anti-CD38 beads. Then we studied the differential expression by qPCR of genes related to MM-MSC interaction (IL-6, IL-8, VEGFA, IL-10, IGF1, HGF, BAFF, GDF15, RANKL, TNFalpha, DKK1, SDF-1). Experiments were performed in triplicate.
Results: Direct co-culture produced the most pronounced transcriptional changes. IL-8 expression was consistently upregulated immediately after co-culture with all MM cell lines (fold change 3.36 ± 1.9 for RPMI8226, 4.02 ± 2.1 for U266, and 3.19 ± 1.2 for MM1.S). This increase was transient, returning to baseline within 48-96 h.
Discussion and Conclusion: Following 72 h of MM exposure, IL-8 was the only gene consistently upregulated across all cell lines, suggesting it may serve as a marker of MSC education under these conditions. The transient nature of most transcriptional changes suggests that induction of many pro-inflammatory genes may be rapid (24h) and short-lived, which may explain why they are inconsistently detected at later time points.

Optimizing AD-MSC Isolation from Lipoaspirates for Translational Medicine: A Comparative Pilot Study

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Introduction: Mesenchymal stem cells (MSCs) represent a promising therapeutic avenue in regenerative medicine, valued for their safety and tolerability. However, their regenerative potential remains a subject of debate, largely because MSCs function as a "living drug" influenced by cell fitness, metabolic state, and population viability. The aim of the current investigation is to compare three AD-MSC isolation methods to identify the most effective protocol for clinical application and translational purposes.
Materials and Methods: Lipoaspirates were obtained from three healthy donors. AD-MSCs were isolated using three distinct techniques: Enzymatic digestion using Liberase (a GMP-grade collagenase/neutral protease blend), mechanical isolation via the Adynazer automated microblade closed system, and by direct isolation from the lipoaspirate. Cell yield and viability were assessed using a Luna automated cell counter and MTT assays.
Results: The enzymatic method provided the highest cell yield with high viability. The mechanical method was significantly faster than enzymatic digestion, though it resulted in a lower overall cell yield. Direct isolation from the lipoaspirate proved to be the least efficient, being both time-consuming and producing the lowest yield.
Discussion and Conclusion: Direct isolation is the most cost-effective, but its low efficiency and the requirement for larger adipose tissue volumes make it less practical for standardized therapeutic applications. For translational medicine, the mechanical microblade system appears to be the most appropriate choice. It is time-efficient, avoids xeno-derived components and enzymatic effects, and maintains a sufficient cell yield for clinical use.

Posters

Prostate cancer stem-like phenotype is associated with enhanced immune evasion and therapeutic resistance

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Short background: Cancer stem-like cells (CSCs) are a specialized niche of tumor cells characterized by self-renewal and differentiation capacity promoting metastasis. In prostate cancer, CSCs contribute to the development of castration-resistant metastatic cancer. Therefore, the investigation of newly found checkpoint inhibitors or therapeutic strategies is essential for treating therapy-resistant cancers. The aim of the present study was to define newly potential targets for personalized immunotherapeutic strategies in stem-like cell-enriched spheroids derived from prostate cancer cell line – PC3.
Materials and Methods: Bone metastatic prostate cancer cell line PC3 (ATCC) was cultivated in RPMI-1640 supplemented with 10% heat-inactivated FBS and antibiotics. Monoclonal antibodies were used to determine surface expression of CD47 and CD326 (EpCAM) flow cytometrically. Long-read nanopore direct RNA sequencing (GridION MK1, SQK-RNA002) with modified library preparation protocol were performed to detect simultaneously non-poly-A long non-coding RNAs (lncRNA) and mRNAs. Data processing was done by FlowJo v10 (BD Biosciences) and Dorado (Oxford Nanopore).
Results: Adhesive PC3 cell line was cultivated under low-binding conditions to promote formation of stem-like cell-enriched spheroids. Flow cytometry analysis of CSC-related markers CD47 and CD326 showed decreased percentage of EpCAM in spheroids, but not in the adhesive wild type. Long-read nanopore direct RNA sequencing showed that most of the genes located on chromosome 21 were differentially expressed in the stem-like enriched population including non-poly-A long non-coding RNAs (lncRNA).
Discussion and Conclusion: Here we showed that the epi-transcriptome profiles of stem-like cell-enriched spheroids might facilitate drug resistance and immune escape. The loss of EpCAM in stem cell-enriched population may contribute to epithelial-to-mesenchymal transition, which is in accordance with upregulated non-poly-A lncRNAs.

The obtained results provide insights into new potential targets that might improve personalized oncology-based immunotherapeutic strategies.

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Electrospun Nanofibers Enriched with Cryoprecipitate as Bioactive Cell-Adhesive Matrices for Personalized Regenerative Medicine

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Background: The development of biomimetic scaffolds that enhance cell adhesion and integration remains a central challenge in regenerative medicine. Cryoprecipitate, a plasma-derived fraction rich in fibrinogen, fibronectin, and growth factors, represents a promising autologous and bioactive material. This study evaluates the adhesive properties of cryoprecipitate and explores its potential as a component of electrospun nanofibrous matrices for personalized applications.

Materials and Methods: Cryoprecipitate was isolated from human plasma by freezing at −80°C for 24 hours followed by centrifugation. The resulting precipitate was resuspended in phosphate-buffered saline (PBS) and used to coat wells of 6-well culture plates. Rat tail collagen was used as a positive control, and albumin-coated wells served as a negative control. Adipose-derived mesenchymal stem cells (ADMSCs) were seeded onto the coated surfaces. Cell adhesion and morphology were assessed at 5 and 12 hours post-seeding using phase-contrast microscopy. To visualize matrix–cell interactions, cryoprecipitate was conjugated with fluorescein isothiocyanate (FITC), and fluorescence microscopy was performed. Additionally, FITC-labeled cryoprecipitate was processed into nanofibers using an electrospinning system.

Results: At 5 hours post-seeding, ADMSCs cultured on collagen-coated wells exhibited rapid attachment and well-spread morphology, while cells on cryoprecipitate-coated surfaces showed partial spreading. By 12 hours, cells on cryoprecipitate demonstrated morphology comparable to those on collagen, indicating delayed but effective adhesion. As expected, no adhesion was observed in albumin-coated controls. Fluorescence imaging revealed dynamic interactions between ADMSCs and FITC-labeled cryoprecipitate, including matrix reorganization and apparent remodeling by the cells. Electrospinning of FITC-conjugated cryoprecipitate successfully produced nanofibrous structures, confirming its processability into scaffold-like architectures.

Discussion: The findings suggest that cryoprecipitate supports mesenchymal stem cell adhesion, albeit with slower initial kinetics compared to collagen. The observed cellular remodeling of the cryoprecipitate matrix indicates active engagement and potential

biofunctionality. Importantly, the successful electrospinning of cryoprecipitate highlights its versatility and applicability in scaffold fabrication. As an autologous material, cryoprecipitate offers advantages in terms of immunocompatibility and personalization.

Establishing an Optimized Protocol for Isolation and Culture of Wharton's Jelly–Derived Mesenchymal Stem Cells toward Comparative Secretome Studies in Normal and Preeclamptic Pregnancies

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Background: Umbilical cord-derived mesenchymal stem cells (MSCs), particularly those isolated from Wharton's jelly (WJ-MSCs), have emerged as an important model for studying fetal-derived cellular responses during pregnancy due to their regenerative potential and immunomodulatory properties, providing a valuable system to study fetal–maternal signaling. Their biological activity is largely mediated by the secretome – a collection of bioactive molecules responsible for paracrine signaling. Dysregulation of these mechanisms may play a role in pregnancy-related disorders, such as preeclampsia. Objective: This study aims to establish a reliable platform for comparative analysis of the secretome from WJ-MSCs, obtained from normal and preeclamptic pregnancies. In the current phase, we focused on developing and optimizing a protocol for cell isolation and culture.
Methods: Umbilical cords were collected post-delivery. Wharton's jelly was isolated, mechanically processed, and subjected to both enzymatic and non-enzymatic digestion to optimize cell isolation efficiency. Cells were cultured in standard MSC medium, and cell attachment, growth kinetics, and morphology were systematically monitored.Results: The optimized protocol enabled reproducible isolation and expansion of WJ-MSCs from all samples. Cells exhibited adherence to plastic surfaces, spindle-shaped fibroblast-like morphology, and robust proliferative capacity. Notably, the non-enzymatic approach outperformed the enzymatic methods in terms of cell yield and culture performance. The established culture system provides a stable foundation for downstream secretome profiling and immunophenotypic characterization.
Conclusion: We present a reproducible, efficient protocol for the isolation of WJ-MSCs, representing a tangible outcome of the current research stage. This platform enables future comparative analyses of secretome profiles from normal and preeclamptic pregnancies, offering insights into disease mechanisms and potential novel regenerative strategies.

Histological analysis of 3D collagen type 1/2 constructs displays cartilage-like tissue formation in vitro

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Collagen constructs are suitable for tissue engineering due to its lack of vascularization and innervation. Furthermore, collagen constructs are 3-dimensional (3D) structures, thus are a step closer to the in vivo application. However, the majority of the literature focuses mainly on the collagen construct produced solely from collagen type 1. It is well established that cartilage main protein is collagen type 2 and that presence of collagen type 1 within the cartilage tissue leads to formation of fibrocartilage and to further degeneration of the hyaline cartilage. This obstacle can be overcome by using collagen type 2 protein for the creation of the collagen constructs, however, this protein has limitations and is recommended to be intermixed with collagen type 1 for stability. A major factor for cartilage formation is also cell number. "Cartilage" differentiation is one of the standard differentiations, used for verifying steaminess in stem cells and involves the use of a higher number of cells. Upon condensation, cells are stimulated with classic chondrogenesis factors to produce an abundance of extracellular matrix, which resembles cartilage tissue. In our investigation, we combine the collagen type 1 and 2 matrix with adipose derived stem cells, in order to observe the effect of 3D structure alone onto the cell behavior. We prepare a mixture of type 1 and type 2 collagens, and combine it with a higher number of cells in collagen gels. Collagen floating fleeces were maintained in complete culture media for a period of 5 days as we visually analyze the remodeling of the collagen matrix and the final histological appearance of the tissue by two different histological stainings. Over the tissue culture period, collagen gels significantly reduced in size and the majority of cells were clustered in the lower side facing the culture media. However, in the rest of the tissue we observed an even distribution of the cells into matrix. The formed structure resembled the territorial matrix of hyaline cartilage and was weakly positive for proteoglycans. Our investigation suggests that formation of 3D structures containing collagen type 2 might be sufficient for the induction of chondrogenesis in stem cells in vitro and thus, our model is suitable for cartilage engineering purposes. However, these findings still have to be proven in vivo.

Poly(sulfobetaine methacrylate) Ionogels Synthesized via Direct Mixing: Emerging Drug Delivery Platforms

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Polymer ionogels are emerging materials composed of a polymer network incorporating ionic liquids, combining mechanical flexibility with high ionic conductivity. Zwitterionic polymers such as poly(sulfobetaine methacrylate) (PSBMA) are particularly attractive for ionogel preparation due to their high hydrophilicity, biomimetic structure, and ability to interact with ionic species. These characteristics make them promising candidates for applications in flexible electronics, sensors, electrochemical devices and recently as drug delivery systems. The present study focuses on the synthesis of PSBMA-based ionogels prepared via the direct mixing method using different crosslinking agents and concentrations, with potential to be applied as drug delivery systems.

Poly(sulfobetaine methacrylate) hydrogels were synthesized by free-radical polymerization using two different crosslinking agents: poly(ethylene glycol) diacrylate (PEGDA) and N,N′-methylenebisacrylamide (MBAA). For each crosslinker, three different concentrations were applied (2, 3, and 4 mol% relative to the monomer). The prepared polymer networks were immersed in two different ionic liquids, 1-ethyl-3-methylimidazolium chloride (EMIM) and 1-butyl-3-methylimidazolium chloride (BMIM), to obtain ionogels. The swelling behavior of the materials was studied as a function of time. The ionic liquid-polymer interaction was evaluated using Fourier Transform Infrared Spectroscopy (FTIR), and the thermal properties of the ionogels were investigated by Differential Scanning Calorimetry (DSC).

PSBMA networks with two different crosslinking agents and varying crosslinking densities were obtained. Swelling kinetics studies showed that both the type and concentration of the crosslinking agent significantly influence the ionic liquids absorption. FTIR analysis showed slight shifts in the characteristic absorption bands for the polymer as well as for the ionic liquids, most likely indicating interaction between them. DSC characterization suggests dependence of the thermal behavior of the obtained ionogels on the crosslinking agent type and quantity as well as on the ionic liquid.

The obtained results demonstrate that the properties of PSBMA-based ionogels depend and could be controlled via the crosslinking density and the type of crosslinking agent used. The direct mixing method represents a simple and effective strategy for incorporating ionic liquids such as EMIM and BMIM into polyzwitterionic networks.

These ionogels show potential for applications in flexible electrochemical devices, ion-conductive materials as well as drug delivery systems.

Circulating Histone Signatures in Plasma Reveal Distinct Profiles Across Solid Tumors and Myelodysplastic Syndrome

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Background: Cancer remains a leading cause of morbidity and mortality worldwide, accounting for more than 20 million deaths annually. A major contributor to cancer-related mortality is late-stage diagnosis. Current gold-standard cancer detection methods often capture a small snapshot of cancer heterogeneity. Liquid biopsies have been extensively studied in recent years and have shown great promise as non-invasive approaches for disease detection, characterization, and monitoring. In this context, complex histone populations are released into circulation and can be detected in biological fluids across various disease settings. Here, we present a rapid, non-invasive liquid biopsy approach based on circulating histones and histone complexes detected in the plasma of adult patients with solid and hematological malignancies.
Materials and Methods: We assessed plasma histone signatures based on individual histones (H2A, H2B, H3, H4, macroH2A1.1, and macroH2A1.2), histone dimers, and nucleosomes using imaging flow cytometry. Samples were obtained from healthy individuals (n = 30) and patients diagnosed with myelodysplastic syndrome (MDS, n = 43), colorectal cancer (CRC, n = 39), lung cancer [non-small cell lung cancer (NSCLC, n = 15) and small cell lung cancer (SCLC, n = 4)], or breast cancer (BC, n = 16).
Results: A general increase in circulating nucleosome levels was observed in the plasma of cancer patients compared with healthy controls, independent of tumor origin. Notably, patients with NSCLC exhibited a significantly distinct histone profile compared with CRC and breast cancer patients, particularly in the abundance of individual histones and histone dimers. Elevated circulating nucleosome levels were also detected in patients with MDS relative to healthy controls. Furthermore, a strong negative correlation between macroH2A1.2 and H2A/H2B/H3/H4 levels and age was observed in healthy individuals, whereas a moderate positive correlation was detected in MDS patients.
Conclusions: Elevated circulating nucleosome levels were consistently observed across all malignancy groups, indicating a promising value as a pan-cancer biomarker. Conversely, individual histones and histone dimers contribute significantly to cancer-type-specific histone profiles, highlighting their potential for tumor classification.

Astrocyte Metabolism and Their Role in Development of Neurodegenerative Diseases

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Background: Astrocytes, representing about 40% of the brain cells, are non-neuronal glial cells that are responsible for forming blood-brain barrier, provide blood flow and nutrients for the neurons, and regulate ion, energy metabolism and synaptogenesis in the brain. They play a dual role in neurodegenerative diseases.
Materials and Methods: Publications from peer-reviewed journals, included in the databases ScienceDirect, PubMed, Taylor and Francis, Springer, and Frontiers, were analyzed.
Results: Astrocytes store glycogen, which structural unit glucose is catabolized into pyruvate and mainly lactate, and the latter is utilized by the neurons via oxidative phosphorylation. They convert the excessive excitatory neurotransmitter α-L-glutamate into the inert α-L-glutamine that is consumed by the neurons and recycled into α-L-glutamate for the neurotransmission. Although most biogenic amines are produced by the neurons, astrocytes can synthesize trace amines, the inhibitory neurotransmitter γ-aminobutyric acid and generally enzymes for the catabolism of aromatic amines, regulating neuronal activity. Astrocytes are the main place in the brain for oxidation of fatty acids, supporting the Krebs cycle activity, and ketogenesis, as ketone bodies participate in the synaptic transmission. Sphingolipids are also produced, stored and catabolized in these cells. Astrocytes participate in the antioxidant neuroprotection reducing peripheral dehydroascorbic acid, generating glutathione and antioxidant enzymes via upregulation of the transcriptional factor Nrf2. Interestingly, they synthesize metal-binding proteins such as ceruloplasmin and metallothioneins that are important for metal ion homeostasis and defense against oxidative stress in the brain. Changes in astrocyte cell distribution, receptor signaling, and metabolic dysfunction, in respect to reduced glucose metabolism, Krebs cycle activity, glutamate uptake, protein synthesis, antioxidant defense, and ion channels, have been observed, in case of depression, dementia, Alzheimer's disease, amyotrophic lateral sclerosis and epilepsy. Additionally, during brain inflammation astrocytes are activated, which triggers stress mitogen-activated protein kinases such as ERK, JNK and p38 kinase, resulting in pro-

inflammatory cytokine production and contributes to astrocyte migration and hypertrophy. Astrocytes also show impaired lipid metabolism presented by mitochondrial dysfunction and accumulation of lipids than fatty acid oxidation for energy supply and accumulation of apolipoprotein E4, as well as decreased cholesterol synthesis, which destroys astrocyte-neuron metabolic coupling.

Discussion and Conclusion: A number of studies reveals the relationship between neurodegenerative disease development and impaired astrocyte metabolism. The modern treatment of neurological disorders has expanded the neuron-targeted approach to the key role of astrocyte phenotype and metabolic activity modulation, and restoring coupling with neurons.

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MicroRNA profiling in metastatic melanoma

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Background: Metastatic melanoma remains one of the most aggressive malignancies, characterized by rapid progression, high metastatic potential, and limited long-term response to targeted and immunotherapies. MicroRNAs (miRNAs) are critical post-transcriptional regulators involved in key oncogenic processes including proliferation, invasion, epithelial-mesenchymal transition (EMT), and metastasis. Dysregulation of specific miRNAs has been implicated in melanoma progression and therapeutic resistance. This study aimed to characterize the miRNA expression landscape in metastatic melanoma and to assess its association with BRAF mutational status.
Materials and Methods: Formalin-fixed paraffin-embedded (FFPE) tissue samples from metastatic melanoma (n=15) and healthy skin controls (n=6) were analyzed. BRAF V600E/Ec mutational status was determined using Real-Time qPCR. Global miRNA profiling was performed using the NanoString nCounter platform, allowing digital quantification of 827 miRNAs. Data were normalized and analyzed for differential expression using nSolver Analysis Software v4.0. Target gene analysis of the most highly overexpressed miRNAs was conducted using experimentally validated interactions from miRTarBase and integrative analysis through miRTargetLink 2.0.
Results: Among the identified differentially expressed miRNAs, miR-146a-5p and miR-4286 showed the highest upregulation, particularly in BRAF-mutant tumors. miR-146a-5p modulates TRAF6 and IRAK1, key nodal proteins of the NF-kB signaling pathway, influencing inflammatory signaling and immune responses, and promoting an immunosuppressive tumor microenvironment. miR-4286 targets PTEN and MAP3K1, controlling PI3K/AKT and MAPK/ERK cascades that regulate proliferation, apoptosis resistance, and metabolic adaptation. Integrative analysis revealed that both miRNAs coordinately target WASF2, a central regulator of actin cytoskeleton remodeling, lamellipodia formation, and cell migration. This dual targeting suggests a convergent mechanism facilitating cytoskeletal dynamics, motility, and invasive potential. Notably, the magnitude of miR-4286 overexpression (fold change >10 in BRAF-mutant samples) correlates with enhanced proliferative and metastatic features, whereas miR-146a-5p upregulation is associated with immune modulation and EMT-like transcriptional programs.
Conclusion: miR-146a-5p and miR-4286 cooperatively regulate gene networks involved in inflammatory signaling, cytoskeletal dynamics, and metastatic progression, with WASF2 as a central convergent target. Their dysregulation, particularly in BRAF-mutant

tumors, underscores their potential as biomarkers and translational therapeutic targets. Integrating miRNA profiling with mutational status provides insights for targeted, combinatorial strategies aimed at simultaneously modulating oncogenic signaling and tumor microenvironment adaptation.

Secretome-Based Bioactive Dressing for Wound Regeneration and Improved Scar Quality in Wistar Rat Model

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Background: Modern wound dressings, incorporating mesenchymal stem cell (MSC) secretome and electrospun nanofibers represent a promising approach to tissue regeneration. However, their effects on healing speed versus scar quality remains incompletely characterized.
Objective: To evaluate whether a bioactive dressing, composed of aligned PLCL nanofibers, loaded with MSC secretome, affects wound contraction rate and scar quality in a full-thickness excisional wound model.
Methods: Sixteen male Wistar rats received two equal full-thickness dorsal wounds each. One wound was treated with the bioactive nanofiber dressing and the contralateral wound served as an untreated control. Wound contraction percentage (WCP) was measured and scar quality was assessed both subjectively, using a modified Vancouver Scar Scale (VSS) and objectively measuring scar dimensions, collagen density analysis and histological evaluation.
Results: Scar quality was significantly superior in nanofiber-treated wounds: VSS score distribution showed 62.5% "good" scars in comparison with 25% for controls, with zero adverse scars in the nanofiber group and 31% adverse scars in controls. Scar size at day 35 was 40% smaller. A significant treatment-by-stress interaction was identified, with stressed animals showing accelerated early healing with nanofibers.
Conclusions: The MSC secretome nanofiber dressing acts primarily as a scar quality modifier rather than a healing accelerator, with an additional capacity to rescue impaired healing in physiologically stressed animals.

In Situ UV-Initiated Synthesis and Characterization of Polysulfobetaine/BMIM Iongels for Biomedical Applications

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Polymer iongels (IG) are soft materials with remarkable properties that recently gained considerable attention in many fields such as flexible electrochemical devices, ion-conductive materials, medical devices, drug delivery systems. They consist of poorly volatile ionic liquid immobilized in a polymer network and have respectively a bi-phase liquid-solid structure. The key properties of IG are the excellent mechanical strength, high thermal and electrochemical stability, extremely good ionic conductivity, nonflammability and nonvolatility. Their physicochemical properties can be easily tuned with the choice of ionic liquid or the polymer.

Polysulfobetaine (PSB) is a biocompatible zwitterionic polymer with excellent antifouling properties that can prevent the formation of bacteria films onto its surface. Moreover, it is thermo- and salt responsive polymer, i.e. it reversibly changes its size upon temperature increase or at presence of electrolytes in the surrounding medium.

The aim of the present study is to obtain PSB ionogels via in situ UV initiated polymerization of sulfobetaine methacrylate (SB) monomer using poly(ethylene glycol) diacrylate (PEGDA) as crosslinking agent in the ionic liquid 1-butyl-3-methylimidazolium chloride (BMIM). These IG have the potential to be further exploited as medical devices or drug delivery systems. To this purpose, we have varied the concentrations of SB monomer and the crosslinking agent PEGDA (respectively 0.5; 1 and 2 mol % with respect to the monomer) preparing solutions in liquified BMIM containing 1 mol % α-ketogluraric acid. The solutions were exposed to UV light to obtain PSB ionogels as a result of the crosslinking polymerization. Fourier Transform Infrared Spectroscopy (FTIR) was used to study the interactions between the SB monomer and the ionic liquid BMIM. The thermal properties of the newly synthesized ionogels were studied via differential scanning calorimetry (DSC).

PSB/BMIM ionogels with three different crosslinking degrees were obtained. FTIR analysis showed slight shifts in the characteristic absorption bands for the PSB as well as for BMIM ionic liquid, indicating an interaction between them. DSC results confirmed the dependence of the PSV IG thermal behavior on the crosslinking agent cocnentration. The in situ polymerization method is a simple and effective strategy for incorporating ionic liquids such as BMIM into polyzwitterionic networks. The obtained ionogels show

potential for applications in flexible electrochemical devices, ion-conductive materials as well as drug delivery systems.

Collagen Substrate Remodeling as a Tool to Assess Paracrine Signaling Between B-Cell Neoplasms and Stem Cells

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Introduction: Collagen remodeling is a key feature of the tumor microenvironment, influencing cancer progression, immune cell behavior, and therapeutic response. In B-cell malignancies such as multiple myeloma and chronic lymphocytic leukemia, tumor cells actively reshape their surrounding matrix, while simultaneously modulating the behavior of neighboring stromal populations, including mesenchymal stem cells (MSCs). Paracrine communication between malignant B-cells and MSCs is known to alter matrix organization, yet quantitative methods for assessing these remodeling events remain limited. Developing reliable in vitro tools to measure substrate remodeling could provide valuable insight into how tumor-derived factors influence stromal cell function and contribute to disease progression.
This study aims to establish a fluorescence-based collagen remodeling assay and apply it to evaluate how secreted factors from B-cell neoplasms affect MSC-mediated matrix remodeling, as well as to characterize the remodeling activity of the tumor cells themselves.
Materials and Methods: Tumor secretome was obtained by culturing B-cell neoplasm lines from multiple myeloma (RPMI 8226) and chronic lymphocytic leukemia (HG-3). The secretome was used to treat mesenchymal stem cells (MSCs) for a period of 72 hours. Fluorescently labeled rat collagen type I, coated on glass, was used to visualize substrate remodeling. After tumor secretome treatment, MSCs were plated on labeled collagen-coated surfaces and cultured to assess their ability to remodel the substrate. Quantification of remodeling was performed by a newly developed automated fluorescence image analysis implemented with CellProfiler software (version 4.2.8). In addition, HG-3 and RPMI 8226 cells were seeded on fluorescent collagen substrates and allowed to attach for 2 h. Supernatants were collected and measured using a standard fluorimeter. Cells and the remodeled substrate were visualized by fluorescence microscopy.

Results: The quantitative collagen remodeling assay revealed increased substrate remodeling by mesenchymal stem cells exposed to secretomes from the B-cell neoplasm lines RPMI 8226 and HG-3. The tumor cells themselves also showed distinct remodeling behaviors, each producing significantly elevated levels of fluorescent collagen fragments.

Discussion and conclusion: These findings indicate that both stromal and tumor cells contribute to collagen remodeling within the tumor microenvironment, albeit through different mechanisms. Stem cells appear to induce a reorganization of the matrix, whereas B-cell tumor lines primarily promote matrix degradation. Overall, this model provides a useful platform for assessing remodeling dynamics in the tumor niche and may support the development of new therapeutic strategies.

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Polymer/Calcium Phosphates Hybrid Materials as Dental Restoratives: An Exploratory Study

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Current dental treatments frequently face challenges with reinfection and inadequate tissue regeneration, particularly in aging patients with compromised healing capacity. This underscores a critical need for multifunctional biomaterials to enhance treatment efficacy for moderate to deep caries. Here, we develop novel hybrids of double quaternary polymer (DQ) poly(N1,N1-diethyl-N2-(2-(methacryloyloxy)ethyl)-N1,N2,N2-trimethylethane-1,2-diaminium chloride iodide) (PDMETMEDA) with in situ-formed calcium phosphates (CaP), offering superior antibacterial activity and remineralization potential.

In this study, PDMETMEDA was synthesized via RAFT polymerization of dimethylaminoethyl methacrylate, followed by a step of its quaternization to attain DQ structure, which was confirmed by ^{1}H-NMR. Its hybrids with calcium phosphates were formed in situ through a two-step process: (1) micro-/nanogel preparation using anionic salts (K_2HPO_4, sodium tripolyphosphate) as crosslinkers, followed by (2) CaP deposition. The micro-/nanogels were characterized for their zeta potential and size by DLS, while CaP phases and morphology were thoroughly analyzed via XRD, ATR-FTIR and SEM-EDX respectively.

Our investigations confirmed the successful DQ PDMETMEDA synthesis, with zeta potential (ZP) rising to +31 ± 5 mV (vs. +23 ± 2 mV for PDMAEMA), indicating enhanced cationic charge due to the quaternization. DLS revealed that the hybrid DQ-CaP micro-/nanogel sizes strongly depend on the DQ-to-anionic crosslinker ratio. XRD showed amorphous CaP or mixed phases formation depending on the initial feed composition. This was corroborated by ATR-FTIR identifying octacalcium phosphate and β-tricalcium phosphate. SEM-EDX analysis displayed uniform spherical particles with homogeneous Ca/P distribution.

These promising results support further development of DQ-CaP hybrids as remineralizing agents for enamel caries, warranting in vitro evaluation on artificial dental models.

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Beta Cell Regeneration During Long-Term Metformin Treatment in a HFD/STZ Rat Model of Type 2 Diabetes

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Background/Aim: β-cell loss in type 2 diabetes (T2DM) involves a reduction in functional mass driven by both apoptosis and cellular dedifferentiation due to chronic metabolic stress. Chronic hyperglycemia and glucolipotoxicity induce endoplasmic stress and apoptotic cell death; many β-cells lose their mature identity. This study investigated the metabolic parameters and morphological patterns of pancreatic β-cell regeneration during long-term metformin treatment in a chronic high-fat diet/streptozotocin (HFD/STZ) rat model.
Methods: Experimental T2DM was induced in rats by HFD combined with STZ injection. Animals received metformin treatment for 28 weeks (initiated at a daily dose of 300 mg/kg, followed by gradual escalation to a final dose of 400 mg/kg). Metabolic parameters (blood glucose, serum insulin, triglycerides, total cholesterol, HDL, LDL, HOMA-B, and TyG) were monitored. Pancreatic tissue was analysed by immunohistochemistry using markers for transcription factors (SOX17, SOX9, PDX1) and expression of hormones: insulin, glucagon, somatostatin, ghrelin, as well as carrier protein aquaporin-7 (AQP7).
Results: Metformin significantly reduced blood glucose from ~22 mmol/L to below 12 mmol/L by week 28 ($p \leq 0.05$) and partially restored serum insulin levels ($p \leq 0.05$). HOMA-B, suppressed in diabetic animals ($p \leq 0.001$), was significantly improved by metformin ($p \leq 0.05$), indicating partial recovery of β-cell function. Elevated HOMA-IR, triglycerides, and TyG index in the diabetic group were significantly reduced following metformin treatment. Histopathological examination revealed islet destruction in the diabetic group, ranging from cytoplasmic vacuolization and focal necrosis to advanced islet atrophy. In the metformin group, morphological evidence of β-cell neogenesis was identified, characterized by small islet-like endocrine clusters exhibiting a budding pattern associated with ductal epithelial elements.
Enlarged insulin-immunoreactive islets consistent with compensatory hypertrophy were also observed. Expanded SOX9-immunopositive ductal progenitor cells and scattered extra- endothelial SOX17-positive cells suggested activation of a pancreatic regenerative response.

PDX1 nuclear expression was preserved within nascent islet structures. Glucagon-positive cells demonstrated diffuse intra-islet distribution, deviating from the normal peripheral pattern. Somatostatin immunoreactivity was identified within fragmented regeneratory islet clusters, reflecting δ-cell participation in islet remodeling. Ghrelin-positive cells were detected within large islet structures, suggesting islet cell plasticity and progenitor-associated regenerative remodeling. These features are rarely observed in the normal adult pancreas. AQP7 was expressed in islet cells, suggesting preservation of glycerol transport capacity and attenuation of β-cell lipoglucotoxicity.
Conclusions: Metformin treatment in the HFD/STZ chronic T2DM model was associated with a multidirectional regenerative response - ductal neogenesis, cellular plasticity, and compensatory hypertrophy in the context of improved glycemic, β-cell functional, and lipid metabolic parameters.
Keywords: aquaporin-7, beta cell, ductal neogenesis, metformin

Assessment of proliferation and osteogenic differentiation of bioprinted mesenchymal stem cells in GelXA BONE and CELLINK BONE bioinks

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Objective: Bioprinting and stem cell-based technologies represent the most transformative advances in regenerative medicine for tissue damage, degenerative diseases, and especially for the treatment of large bone defects that cannot heal on their own. Bone tissue printing is a rapidly developing field that would overcome the limitations of traditional grafts, creating personalized implants. Mesenchymal stem/stromal cells (MSCs) have emerged as particularly promising candidates due to their multipotent differentiation potential, immunomodulatory properties, paracrine signaling, and relative ease of isolation and expansion.
The aim of this study was to compare the proliferation and osteogenic differentiation in vitro of BM-MSCs printed with two osteoconductive bioinks.
Materials and methods: GelXA Bone and CellInk Bone bioinks (CELLINK) mixed with $1x10^6$ BM-MSCs/ml were printed using BioX (CELLINK) according to the manufacturer's specifications. The bioprinted 3D constructs were cultured in DMEM or osteoinductive media. Cell proliferation was measured by Alamar blue. Cell morphology and survival were visualized by a live/dead kit. MSCs cultured in osteoinductive medium were analyzed for differentiation by measuring alkaline phosphatase (ALP) activity and assessing gene expression of ALP, Runt-related transcription factor 2 (RUNX2), and osteocalcin (OCN) at 7, 14, and 21 days.
Results: We found that MSCs cultured under standard conditions retained their proliferative potential, with growth observed for up to 21 days with both bioinks. The increase in cell number was also confirmed by live/dead cell staining images. We found that there was a negligible number of dead cells on the day after printing, as only single dead cells were subsequently detected. These images also revealed a difference in cell morphology. MSCs in GelXA prints were larger and had a fibroblastoid shape, in contrast to CellInk prints, where MSCs were smaller and round. Osteogenic differentiation in MSCs in the two bioinks also showed differences. ALP activity increased in CellInk prints during the differentiation process, while in GelXA prints it was highest on day 7 and decreased thereafter. This trend was confirmed by ALP mRNA expression. RT-PCR analysis of CellInk prints revealed low RUNX2 expression and absence of OCN at the mRNA level. In contrast, GelXA prints showed increased of RUNX2 with time and OCN gene expression was detectable on day 21.

In conclusion, we can summarize that MSCs successfully proliferate and differentiate in both bioinks, but differences in morphology and dynamics of expression of osteogenic markers should be considered in terms of the functionality of bioprinted cells in regenerative processes.

Impact of post-translational collagen oxidation and glycation on mesenchymal stem cell interaction and matrix remodeling

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Short background: Mesenchymal stem cells (MSCs) play a central role in regenerative medicine due to their ability to remodel and reorganize the extracellular matrix (ECM). Collagen type I is a major structural component of the ECM, and its biochemical integrity is essential for proper tissue homeostasis. Post translational modifications such as oxidation and early glycation can alter collagen's structure, stability, and susceptibility to proteolytic remodeling, contributing to the development or progression of various pathological conditions.
Objective: To investigate how specific post translational modifications—namely oxidation and early glycation of type I collagen—affect MSC behavior in vitro, with a particular focus on cell–matrix interaction and collagen remodeling capacity.
Materials and methods: Type I collagen was isolated from rat tail tendon (RTC) and subjected to controlled oxidation or early glycation using established protocols. The extent of glycation was quantified using the TNBS assay, which revealed a significant reduction in free amino groups per tropocollagen molecule after 5 days of glycation. Adipose derived MSCs (ADMSCs) were cultured on native, oxidized, or glycated collagen substrates. Their remodeling activity was evaluated morphologically, assessing protein translocation, fibrillar reorganization, and evidence of pericellular proteolysis.
Results: ADMSCs interacted robustly with native adsorbed collagen, inducing marked remodeling characterized by mechanical translocation of collagen, formation of fibril like structures, and the appearance of dark proteolytic bands indicative of active matrix degradation. In contrast, both oxidation and glycation significantly impaired MSC–collagen interaction. Modified collagen substrates showed reduced remodeling, diminished proteolytic band formation, and altered cell morphology. Glycation in particular appeared to disrupt collagen's structural organization, further influencing MSC adhesion, spreading, and remodeling behavior.
Conclusion: Post translational modifications of collagen, including oxidation and early glycation, substantially compromise collagen stability and interfere with MSC mediated remodeling. These modifications reduce available proteolytic sites, promote collagen

fragmentation, and alter cell–matrix interactions. Understanding how modified ECM components influence stem cell behavior is essential for improving regenerative strategies, especially in pathological environments characterized by oxidative stress or dysregulated glucose metabolism.

Paracrine Signals from B-cell Neoplasms Induce Reprogramming Toward a Cancer Associated Phenotype in Stem Cells

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Introduction: The tumor microenvironment is shaped not only by malignant cells but also by the surrounding stromal populations that they reprogram through paracrine signaling. Among these stromal components, mesenchymal stem cells (MSCs) are particularly responsive to tumor-derived cues, acquiring features characteristic of cancer-associated MSCs (CA-MSCs). In B-cell malignancies such as chronic lymphocytic leukemia (CLL) and multiple myeloma (MM), accumulating evidence suggests that soluble factors released by tumor cells play a central role in driving stromal adaptation and supporting disease progression. Despite this, experimental models that allow controlled investigation of paracrine interactions between B-cell neoplasms and MSCs remain limited, especially when it comes to assessing the durability of these changes. This study aims to model and quantify MSC reprogramming driven by B-cell neoplasm secretomes and evaluate its persistence after secretome removal.
Materials and Methods: Mesenchymal stem cells (MSCs) were treated for 72 h with cancer-cell-secrfetome (CCS) obtained from the B-cell lines HG-3 (CLL) and RPMI 8226 (MM). Total protein content in CCS was quantified using the Bradford assay. To assess both induced and residual effects, MSCs were subsequently cultured for an additional 72 h in standard medium. Phenotypic changes were evaluated through assays of proliferation, senescence (SA-β-gal), and migration (in vitro wound-healing), along with a viability assessment using Calcein/propidium iodide staining.
Results: Exposure of MSCs CCS resulted in marked functional reprogramming. Treated MSCs displayed a two-fold increase in proliferative rate compared to controls, a 3÷4-fold rise in senescent cells, and accelerated migration. Importantly, cell viability remained largely unchanged. When MSCs were subsequently cultured in secretome free medium, most of these phenotypic alterations persisted, indicating that the induced reprogramming is at least partially irreversible.
Discussion and Conclusion: These findings demonstrate that soluble factors released by RPMI 8226 and HG-3 cells profoundly influence MSC biology, driving them toward

a phenotype resembling cancer associated MSCs. The sustained changes observed after secretome withdrawal highlight the robustness of this reprogramming and suggest that tumor induced stromal alterations may persist even in the absence of continuous malignant signaling.

The developed model effectively captures the paracrine influence of B-cell neoplasm lines on MSC function and provides a controlled platform for dissecting stromal reprogramming mechanisms. Its ability to reveal both immediate and lasting effects makes it valuable for fundamental studies of tumor-stroma communication and for screening therapeutic strategies aimed at disrupting paracrine signaling within the tumor microenvironment.

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Application of Electrochemotherapy in 3d Bioprinted Colorectal Cancer Models - a Pilot Study

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Introduction: Colorectal cancer (CRC) mortality rates continue to increase, positioning CRC among the top three most prevalent oncopathologies with fatal outcomes. Drug resistance to current therapies remains a major obstacle, contributing to persistently high mortality, therefore necessitating frequent modifications in treatment protocols. Electrochemotherapy (ECT), which combines electroporation-induced pore formation in cell membranes with chemotherapeutic agents, has the potential to enhance therapeutic efficacy. This study aimed to validate a novel ECT approach using 3D bioprinted CRC models that closely mimic the tumor microenvironment as a platform for evaluating chemotherapeutic agents.

Materials and Methods: Standard CRC cell lines (HCT-116 and Caco2) were bioprinted using RGD bioink (with BioX Cellink, Sweden). On day 8, electroporation was performed with the Clinivet device (IGEA, Italy) according to a clinical protocol: 8 pulses, 100 ms duration, 5 kHz frequency, within the reversible electroporation range (below 1000 V/cm). Electroporation efficiency was evaluated immediately by microscopic counting of propidium iodide positive cells, while cell viability was determined by MTT assay after 72 hours. For ECT, the IC50 values of Bleomycin were applied (1.71 μg/ml for HCT-116 and 6.15 μg/ml for Caco2).

Results: Both CRC cell lines exhibited a clear voltage-dependent reduction in metabolic activity and viability, with 420 V (700 V/cm) identified as the optimal electroporation voltage. Bleomycin administered after ECT produced a higher cytotoxic effect. Additionally, in both CRC 3D models following ECT with Bleomycin, the number of Ki67-positive cells was markedly reduced, while Caspase 3 levels increased, indicating inhibited cell proliferation, enhanced cell death and activation of apoptosis.

Discussion and Conclusions: The findings indicate that ECT significantly enhances the antitumor efficacy of Bleomycin in 3D bioprinted CRC models. The established 3D bioprinting platform together with ECT, provides a robust foundation for testing both standard chemotherapeutic agents or natural compounds. These results underscore the value of integrating 3D bioprinting and ECT as a powerful preclinical platform for CRC research and therapeutic optimization.

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A murine embryonic fibroblast model to study the etiology of Rahman syndrome

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The Rahman syndrome (RMNS) is a recently identified, very severe neuro-developmental disorder. RMNS patients exhibit a characteristic phenotype along with hypothyroidism, abnormal dentition, behavioral issues, skeletal and cardiac anomalies, as well as strongly expressed intellectual disability. RMNS is an as-yet poorly defined syndrome causally linked to germline frameshift mutations in one of the alleles of the linker histone H1.4 (H1E). The mutant protein has an altered C-terminal tail with significantly reduced positive charge. The H1E mutations may affect the overall epigenetic landscape of chromatin and several vital nuclear processes, including transcription and cell cycle progression. However, in-depth analysis of the etiology and the epigenetic landscape of RMNS is missing.

We use mouse embryonic fibroblasts (MEFs) as a model system, prepared from genetically modified mouse strains in which either one or both H1.4 alleles are substituted with the RMNS H1.4 mutant sequence. We use basic molecular biology methods like RT-PCR, Western blot, immunofluorescence, etc., in combination with high-throughput methods like RNA-seq to validate and go in depth into the effect of the RMNS mutation.

We confirmed the presence of a mutant histone and a twofold difference in its expression between homozygous and heterozygous mutants in the MEFs. We characterized in depth the MEFs, having either one H1.4 allele (heterozygous) or both H1.4 alleles (homozygous) replaced with the RMNS mutant H1.4, and confirmed their suitability as a model system for studying RMNS. Immunofluorescence staining by gamma H2AX hints at increased genome instability in the presence of H1E mutation. The effect of the mutation is dosage-dependent, since in the homozygous mutant we observe many more genes with altered expression (1665 significantly affected genes in heterozygous vs. 6012 in homozygous mutant).

The combined data suggest that RMNS mutations promote an aberrantly changed chromatin state, potentially leading to the dysregulation of gene expression that may drive RMNS pathology.

Isolation and Functional Assessment of Jellyfish-Derived Biomaterial

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Marine jellyfish are an underused but promising source of collagen, of low immunogenic potential and good biocompatibility, offering potential advantages over traditional mammalian-derived biomaterials. This study examined collagen extracted from the Black Sea jellyfish Rhizostoma pulmo to assess its suitability for tissue engineering and wound-healing applications.

Collagen was obtained using an acid-soluble extraction method and compared with a standard mammalian collagen reference collagen (RTC). The extracted jellyfish collagen (JFC) yield was approximately 5-10 mg per gram of tissue. Structural characterization was performed through UV-VIS and FTIR spectroscopy and SDS-PAGE, as well as a collagenolytic assay. The results confirmed that the purified jellyfish collagen maintained key molecular features required for biomedical use, including preserved triple-helical organization and characteristic molecular weights.

Biocompatibility was evaluated using human adipose-derived mesenchymal stem cells (ADMSCs). These assessments included cell adhesion behavior, spreading morphology, focal adhesion (FA) formation, (FA per cell JFC: 54±18 vs RTC: 47±20), and overall viability. ADMSCs showed strong compatibility with the JFC collagen, exhibiting cell-spreading areas (CSA): JFC: 4,246±2,005 μm^2 vs RTC: 4,886±2,643 μm^2, $p>0.05$) and adhesion patterns comparable to mammalian collagen. Cell viability remained above 95% after 24 hours, demonstrating the collagen's non-cytotoxic nature.

Electrospinning nanofiber scaffolds combining jellyfish collagen with PLCL were produced to evaluate their potential in wound-healing platforms. These nanofibers exhibited a fine, ECM-like architecture and supported efficient, directional cell migration. In an in-vitro wound model, the scaffolds facilitated 95 ± 3% wound closure within 24 hours, closely matching the fibrils of mammalian ECM. In contrast, RTC-based scaffolds showed a coarser fiber structure, suggesting different mechanical and structural advantages depending on the intended application.

Overall, R. pulmo collagen demonstrates structural stability and strong compatibility with stem cells. Its fine fiber architecture makes it particularly advantageous for applications such as cartilage repair, soft tissue regeneration, and wound healing, where

delicate scaffolds and biomimetic extracellular matrix structures are essential. These findings highlight marine jellyfish collagen as a promising, sustainable alternative to mammalian collagen in regenerative medicine.

Applications of 3D Printing and Medical Image Segmentation in Surgical Planning and Training

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Advances in medical imaging, image processing, and additive manufacturing have created new opportunities for improving surgical planning and medical education. By transforming radiological data into patient-specific three-dimensional representations, clinicians can better understand complex anatomical structures and pathological conditions before entering the operating room.
In our 3D printing laboratory, we apply medical image segmentation and 3D printing technologies to generate anatomically accurate digital and physical models that support clinical decision-making and hands-on training. These models enable improved spatial visualization of anatomical relationships and allow surgeons to explore operative strategies in a tangible way.
The presented work demonstrates how the integration of medical imaging and additive manufacturing can enhance preoperative preparation, facilitate the visualization of pathological structures, and provide realistic training tools for developing surgical skills. Together, these approaches highlight the growing role of patient-specific modeling and anatomical replicas in modern surgical practice and education.

Application of collagen-based bioinks for chondrocyte differentiation in 3D bioprinted human stromal-vascular fraction (SVF) cells - comparative gene expression analysis.

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Introduction: Cartilage regeneration is notoriously difficult and new tissue engineering approaches are needed. We present the chondrogenic potential of two novel bovine collagen type I-based bioinks on SVF cells and compare the gene expression changes to the gold standard 3D pellet culture system.
Materials and methods: Two collagen type I-based bioinks were prepared with 8 million cells/ml of hTERT A41hWAT-SVF cells (immortalised white adipose tissue stromal vascular fraction cells) and either one of two hydrogels - containing 2% bovine collagen or containing 2% collagen and 1% hyaluronic acid (HA) (w/v) was used. Cells were bioprinted using an extrusion-based 3D bioprinted (BioX, Cellink, Sweden) at ~10 kPa pressure in 2-layer discs with diameter of 5mm and were cultured for 2 weeks prior to RNA extraction and further gene expression and histomorphological analysis. Patient-derived SVF cells isolated from lipoaspirates were also 3D bioprinted to validate the biocompatibility of the hydrogels and the feasibility of the approach. RNA was extracted from SVF cells grown in 3D pellets, from SVF cells grown in monolayer (2D culture), and from collagen and collagen+HA bioprints (from at least 2 bioprints in duplicates). After RNA-sequencing, comparisons of gene expression were made between (1) 3D spheroids vs 2D cultures, (2) collagen bioprints vs 2D cultures, and (3) collagen+HA bioprints vs 2D cultures.
Results: Both collagen and collagen+HA hydrogels showed excellent biocompatibility with SVF cell lines and patient samples for at least 3 weeks of cell culturing after 3D bioprinting. RNA-seq gene expression analysis revealed that all three approaches – (1) 3D aggregates/spheroids and bioprinting with (2) collagen or (3) collagen+HA demonstrate enrichment for chondrocyte differentiation, albeit to a different degree

Only in the standard 3D spheroid cultures we noticed **chondrocyte** hyperthrophy signatures, while the two bioprinting approaches did not reveal any gene expression signs of this unwanted phenomenon. The addition of HA led to enhanced enrichment for GAG biosynthesis. The further functionalisation of the bioink showed augmented gene expression signatures for collagen fibril organisation), and for extracellular matrix and function organisation.

Discussion and conclusion: The observed differences provide a strong rationale in support of the advantages of 3D bioprinting over 3D cultures and suggest improved extracellular matrix production with the addition of HA in the bioinks.

Differential caspase-1 activation induced by SARS-CoV-2 ORF3a mutants reveals variant-dependent inflammasome signaling in human endothelial cells

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Short background: Endothelial dysfunction and excessive inflammasome activation are key contributors to severe COVID-19 and Long COVID-associated vascular pathology. The SARS-CoV-2 accessory protein ORF3a has been implicated in inflammasome signaling and pyroptosis; the functional impact of naturally occurring ORF3a mutations on endothelial inflammatory responses remains unclear. This study evaluated the ability of lineage-linked ORF3a variants to modulate caspase-1 activation in human microvascular endothelial cells.
Materials and Methods: Human microvascular endothelial HULEC-5a cells were transfected with 0.1 μg/μL plasmids encoding wild-type ORF3a (Wuhan-Hu-1) or mutant constructs (L106F, Q57H, T223I, A99V+Q57H, G172V+Q57H, Y264C+Q57H) for 24 hours. Caspase-1 activity was detected using the FAM-FLICA fluorescent assay and Hoechst nuclear staining, followed by confocal imaging. Quantitative single-cell analysis was performed using Imaris and CellProfiler. Nigericin treatment served as a canonical NLRP3-mediated pyroptosis control. Statistical evaluation included Kruskal-Wallis testing with Dunn-Bonferroni corrections and mixed-effect models.
Results: ORF3a expression induced robust caspase-1 activation compared with untreated controls. Two distinct activation phenotypes were observed, indicating both diffuse cytosolic and inflammasome-type signaling. Significant differences were detected among variants ($p<0.0001$). The T223I mutant demonstrated the strongest pro-inflammatory activity, increasing the probability of inflammasome-positive cells. Double mutants containing Q57H (A99V+Q57H, Y264C+Q57H, G172V+Q57H) also significantly enhanced caspase-1 activation. The Wuhan reference strain produced moderate responses, whereas L106F showed no significant effect. Mixed-effect modeling confirmed preferential diffuse cytosolic inflammasome signaling for A99V+Q57H and the largest overall effect for T223I. Genomic surveillance showed that the most inflammatory mutations were enriched in viral variants that dominated during major epidemic waves.
Discussion and Conclusion: These findings establish a hierarchy of ORF3a mutant inflammatory potency and demonstrate that viral genetic variation directly modulates endothelial inflammasome signaling. Variant-dependent caspase-1 activation provides

a mechanistic link between SARS-CoV-2 evolution and vascular inflammation, highlighting ORF3a as a potential therapeutic target for preventing endothelial injury and post-COVID complications.

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Artificial Intelligence-Assisted Monitoring of Induced Pluripotent Stem Cell Cultures for Standardised Regenerative Medicine

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Background: Induced pluripotent stem cells (iPSCs) represent a promising platform for regenerative medicine due to their ability to differentiate into multiple functional cell types while retaining patient-specific genetic characteristics. Clinical translation of iPSC-derived therapies remains constrained by variability in culture conditions, subjective morphological assessment, and challenges in maintaining reproducible quality during large-scale manufacturing. In routine practice, colony morphology, confluency, edge patterns, and molecular markers indicate pluripotency and culture stability, yet manual evaluation is labour-intensive and prone to inter-observer variability. Artificial intelligence (AI), particularly deep learning-based computer vision and machine learning (ML), offers opportunities to automate monitoring of stem cell cultures through objective analysis of cellular morphology, growth dynamics, and differentiation trajectories, supporting more consistent production of clinical-grade cells.
Materials and Methods: A structured literature analysis of studies published between 2020 and 2026 evaluated emerging AI applications in iPSC culture monitoring and bioprocess optimisation. The analysis reviewed convolutional neural networks (CNNs), Vision Transformers (ViTs), and transfer-learning models for automated classification of colony morphology from phase-contrast images. Methods included supervised predictive models for differentiation outcome prediction and unsupervised dimensionality-reduction techniques, including principal component analysis (PCA) and UMAP, applied to multi-omics datasets. Particular attention was given to computational frameworks capable of detecting early pluripotency loss, identifying spontaneous differentiation, and optimising culture parameters.
Results: Deep learning-based image analysis achieved 90-95% accuracy in distinguishing pluripotent colonies from partially differentiated or abnormal populations in standard microscopy images. CNN-based models detected subtle morphological changes associated with early differentiation stages prior to measurable changes in molecular pluripotency markers. Multimodal ML pipelines integrating imaging features with transcriptomic and proteomic datasets further enhanced the precision of cellular state detection. Additionally, predictive ML models including Random Forest and Gradient Boosting algorithms, applied to culture parameters (media composition, mechanical microenvironment, growth-factor timing) improved

cardiomyocyte and neural progenitor yield. Digital twin bioprocess modelling frameworks utilising these models successfully forecast culture performance and reduce batch-to-batch variability.

Discussion and Conclusion: Integrating artificial intelligence into iPSC research represents a critical step toward scalable and standardised regenerative medicine. By replacing subjective visual inspection with quantitative, deep-learning-derived metrics, these systems improve reproducibility and support Good Manufacturing Practice (GMP)-compliant workflows. AI-assisted quality control and predictive bioprocess monitoring are likely to become essential tools for ensuring the safety and regulatory compliance of advanced cellular therapies in clinical settings.

Announcement and Invitation

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