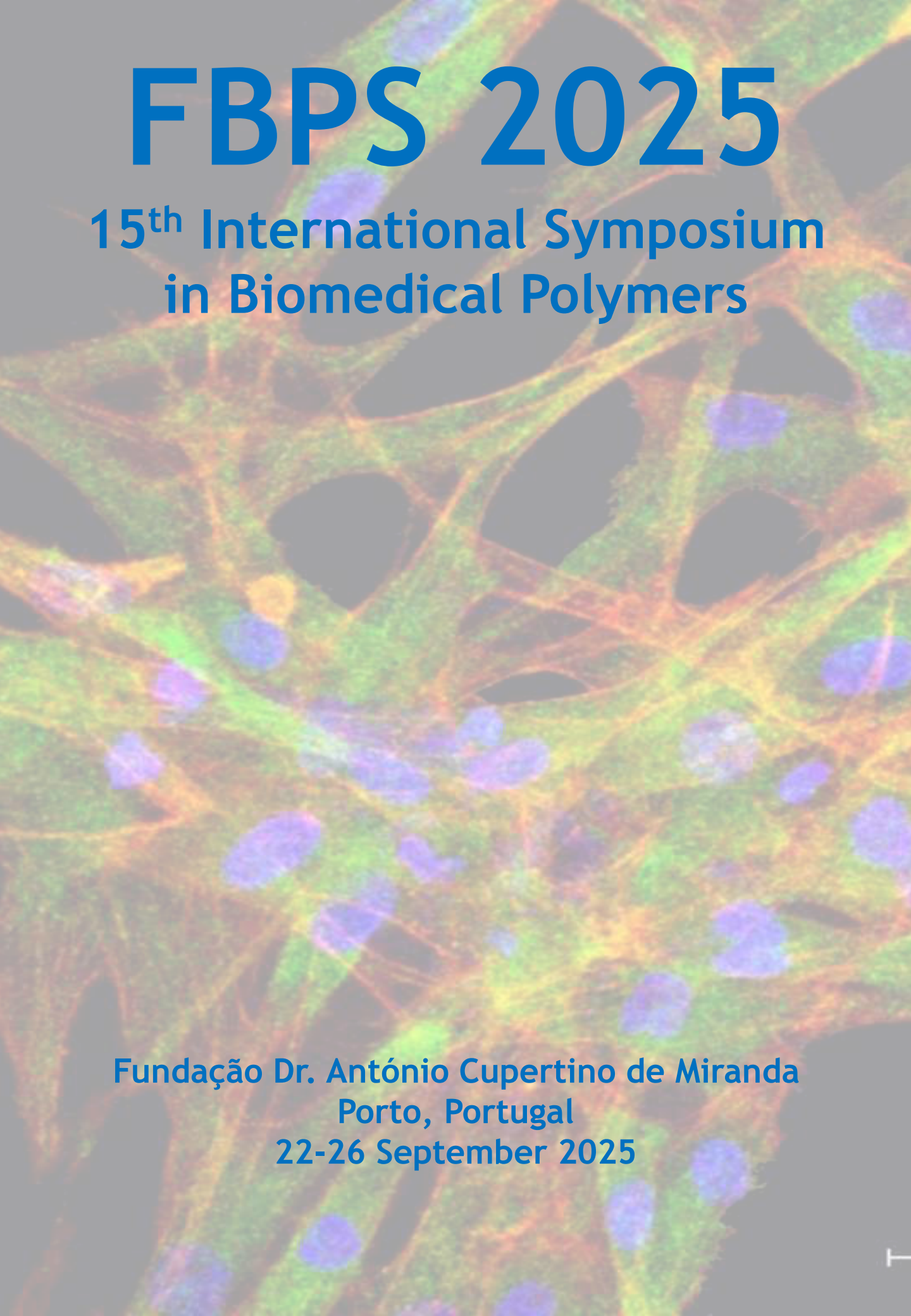
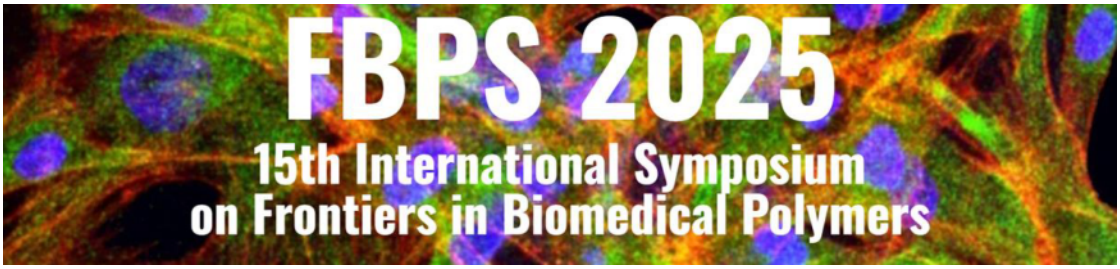
FBPS 2025

15th International Symposium in Biomedical Polymers



Fundação Dr. António Cupertino de Miranda
Porto, Portugal
22-26 September 2025



CONFERENCE HIGHLIGHTS

The 15th International Symposium in Biomedical Polymers, will be held from the 22th to the 26th of September, 2025, in Porto, Portugal. This meeting is the 15th edition of a series of conferences organized by the International Scientific Committee over the past 30 years in different continents, with an interruption due to Covid. This meeting will commemorate our 30th years of organizing this very successful meeting. In addition to honor the founders of the meeting we will have special sessions to honor the recently deceased Prof. Julio San Roman and Prof. Allan Hoffman. Julio was one of the most active members of FBPS and one of our organizers. Allan was one of the most supportive members in the community and an inspiration for many years for all of us working on biomedical polymers.

This meeting will be, as usually in this series, a great opportunity for discussions of past, present, and future research on bioactive and functional polymers for advanced biomedical applications and tissue engineering. A very relaxed and cooperating atmosphere, both on science and on the social events, will be implemented. An exciting and looking forward scientific program will cover basic to applied themes, focusing also on advanced post-graduate training and on entrepreneurship opportunities. The meeting will also serve as a forum for students, postdoctoral fellows and established scientists from different countries to exchange ideas, broaden knowledge and develop long lasting collaborations.

Looking forward to meeting you in Porto!

The conference chair

Prof. Rui L. Reis, FBPS Committee Member & FBPS 2025 Organizer

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GENERAL INFORMATION

All the information contained in this book is accurate at the time of its publication. The Conference Organizers reserve the right to alter the programme and the associated events as circumstances dictate.

ORGANIZING COMMITTEES

CONFERENCE CHAIR

Prof. Rui L. Reis, FBPS Committee Member & FBPS 2025 Organizer

FBPS COMMITTEE MEMBERS

Rui L. Reis
University of Minho, Portugal

Claudio Migliaresi
University of Trento, Italy

Daniel Cohn
Hebrew University, Israel

David Kaplan
Tufts University, USA

Antonella Motta
University of Trento, Italy

Teruo Okano
Tokyo Women's Medical School, Japan

Gilson Khang
Jeonjuk National University, Korea

LOCAL ORGANIZING COMMITTEE

Albina Franco	Luísa Rodrigues
Albino Martins	Márcia Rodrigues
Carlos Guimarães	Marta Casanova
César Casanova	Miguel Oliveira
Emanuel Fernandes	Natália Alves
Filipe Ribeiro	Nuno Neves
Helena Ferreira	Raquel Maia
Isabel Leonor	Ricardo Pires
Iva Pashkuleva	Tiago Silva
Liliana Gomes	Vitor Correlo
Lucília Silva	

SECRETARIAT

Ana Guerra | Ariana Santos

CONFERENCE VENUE

The conference will be held at the Dr. António Cupertino de Miranda Foundation, in Porto (Portugal), at the Auditorium II.
Dr. António Cupertino de Miranda Foundation was set up in 1964. This Foundation is located at "Avenida da Boavista", the longest avenue in Porto that is more than 5 km in length and crosses 6 neighbourhoods!

Fundação Dr. António Cupertino de Miranda
Avenida da Boavista, 4245
4100-140 Porto
Portugal

Telephone (+351) 226 101 189
Fax (+351) 226 103 412
General e-mail: geral@facm.pt

GETTING TO AND FROM THE VENUE

You can use public transportation (bus no. 502 and 504) or private transportation (taxi) to get to the congress venue.

By car
From the south: Take A1 motorway in the direction of Porto, continue by Avenida da Boavista until Dr. António Cupertino de Miranda Foundation.

From the north: A28 motorway from Valença. A3 motorway from Braga. A7 motorway from Guimarães.

Once in Porto: Dr. António Cupertino de Miranda Foundation is located almost at the end of Avenida da Boavista (Boavista Avenue), in front of the Parque da Cidade (City Park). This avenue connects the ocean, near the famous "Castelo do Queijo", an awesome fortress near the beach, with the Rotunda da Boavista (Praça Mouzinho de Albuquerque), next to the beautiful "Casa da Música", a masterpiece designed by the Dutch and Pritzker Prize winner architect Rem Koolhaas.

By plane:
16 Km/20 minutes away from Francisco Sá Carneiro Airport (OPO).

GPS Coordinates: 41º 9' 54" N (Latitude), 8º 40' 24"W (Longitude)

REGISTRATION AND INFORMATION DESK

All attendees must be registered for the conference. Admission to the conference is permitted only to those wearing the official conference badge. If a name badge is misplaced, please contact the registration desk.

Certificate of Attendance will be provided to all registered participants through email after the completion of the conference.

The information/registration desk will be located at the Foyer of the Auditorium II in the first day of the conference and will be open during the following days.

Internet
Wireless network at Dr. António Cupertino de Miranda Foundation will be available. Please address information desk to get the username and password, if necessary.

Lunch
Lunch planned for the conference is included in the registration fee and will be served at the restaurant of the Dr. António Cupertino de Miranda Foundation.

Smoking policy
From the 1st of January 2008 legislation was introduced in Portugal, which makes it forbidden to smoke in all public places. This includes cafes, bars and restaurants (excluding those with signalized smoking areas). Smoking is only allowed outside the Venue building.

Photography policy
Recording and photographing conference presentations will not be allowed.

Electricity supply
220V is the standard power supply throughout Portugal. If you need a plug or a power adapter, you may find in electronic specialty retailers or ask in the registration desk.

Transportation
In Porto, there is metro and bus that lets you travel through the city centre. If you want to travel by bus/metro, the tickets (andante) prices for one day are from 7,50€ on. The Bus 502 and 504 leave you in the Conference Venue, the stop is "Parque da Cidade".

Airport: www.ana.pt
Train: www.cp.pt
Metro: www.metrodoporto.pt
Bus: www.stcp.pt

Taxis operate 24 hours and can be ordered from the Event Venue or from your hotel. Taxis can be hailed in the streets if they have the green light on in the front that says “TAXI”. Do not use unlicensed taxis, which are ordinary cars and drivers looking for business, offering taxis in the street.

Renting a car can be a very nice solution if you want to stay in a place "far" from the centre. It is not very expensive to rent a car but, if you want to feel the city, you can make longer trips, because the city centre has a lot of small streets, that you can only enjoy walking.

Weather
Please visit the Portuguese Meteorology Institute website: www.ipma.pt
Or the worldwide known: www.weather.com

Tourism and leisure
The conference venue is located in the very heart of the city of Porto. Just go out and enjoy! To know more about the city, please visit the following websites:

www.portoturismo.pt
www.portoenorte.pt
www.lonelyplanet.com/portugal/the-north/porto/things-to-do

You can also buy Time Out Porto to know what happening this month in the city.

Currency
Portugal uses the Euro (€). Traveller's cheques can be exchanged for cash in banks and exchange bureaus.

Emergencies
Police, ambulances, fire services: Dial 112.

Liability
The Organising Committee of the conference accepts no liability for participant personal injuries or loss/damage to personal property either during or as a result of the Conference, or during the social events. They are entitled to make any changes, modifications or omissions with respect to the information published in this book.

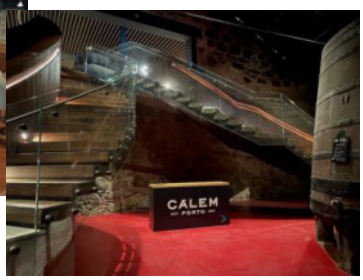
Insurance
The Conference Organisers cannot accept any responsibility for personal accidents and damage to the private property of Conference and Exhibition Delegates.

SOCIAL PROGRAM

Conference Dinner will take place @Cálem Cellars.
25th September at 20h00
Avenida Diogo Leite nº344 – 4400-111 Vila Nova de Gaia

Experience Room

Cálem Cellars present themselves as a privileged place for several cultural, social and business events. Apart from being located in one of the most beautiful places of Vila Nova de Gaia, with a wonderful view upon the historical Ribeira do Porto, these cellars are the perfect place to hold meetings, exhibitions, conventions, dinners or wedding ceremonies.



SCIENTIFIC INFORMATION

KEYNOTE PRESENTATION FORMAT

20 minutes presentation
5 minutes discussion

ORAL PRESENTATIONS INFORMATION

The code attributed to the Oral Presentations in the program corresponds to the code given in this proceedings book in the abstracts list.
10 minutes presentation
2.5 minutes discussion

PRESENTATIONS UPLOAD

The conference presentations will all take place at the Auditorium II of Dr. António Cupertino de Miranda Foundation.

Personal computers or USB pen drive will be allowed for the presentation. Accepted formats: PowerPoint (.pptx) or PDF and all presentations must be prepared in 16:9 format.
There will be a Speakers Preparation Desk identified in the information/registration desk on the ground floor where all speakers **MUST** upload their presentation as soon as possible with the deadline as in the following schedule:

SESSION	Upload deadline	
	Day	Deadline Time
Keynotes Presentations (22.09 | Afternoon)	22/set	14h00
Keynotes Presentations (23.09 | Morning)	22/set	16h30
Oral Presentations (23.09 | Morning)	22/set	16h30
Keynotes Presentations (23.09 | Afternoon)	23/set	11h05
Oral Presentations (23.09 | Afternoon)	23/set	11h05
Keynotes Presentations (24.09 | Morning)	23/set	16h30
Keynotes Presentations (24.09 | Afternoon)	24/set	11h05
Oral Presentations (24.09 | Afternoon)	24/set	11h05
Keynotes Presentations (25.09 | Morning)	24/set	16h30
Oral Presentations (25.09 | Morning)	24/set	16h30
Keynotes Presentations (25.09 | Afternoon)	25/set	11h05
Keynotes Presentations (26.09 | Morning)	25/set	16h30

POSTER SESSIONS & SCHEDULE

Posters will be presented during the official Poster Sessions as part of the scientific program and will be divided across the three days. Each poster abstract will be assigned to one of the poster sessions.

Session Dates:

Session 1-Core Biomaterials, Nanomedicine & Tumor Models: Tuesday, 23rd September 2025

Session 2- Hydrogels, Wound Healing & Regenerative Biology: Wednesday, 24th September 2025

Session 3- Advanced 3D Bioprinting & Marine/Sustainable Biomaterials: Thursday, 25th September 2025

Presentation Timing:

Poster presentations will take place during the coffee breaks of each session day. Presenters are expected to be present at their posters during these breaks to engage with attendees and respond to questions.

Poster Setup & Removal

Posters should be set up ideally no later than the Opening Ceremony (Monday, 22nd September 2025) and remain in place for the duration of the symposium.

Suitable fixing material will be provided by the organizers. If the posters are made of a different material than paper (e.g. cloth), organizers do not guarantee that the posters will remain in place.

Poster boards and poster card numbers will be provided at the poster presentation area; presenters must stick their posters on the assigned poster board (Poster Number Assigned in the Final Program).

Posters must be removed at the end of the symposium, on Friday 26th September 2025.

The organizers will remove any posters left behind and may not be returned.

CONFERENCE PROGRAM

	Day 1 Monday 22	Day 2 Tuesday 23		Day 3 Wednesday 24		Day 4 Thursday 25		Day 5 Friday 26
09:00|09:25		Allan Hoffman	Session 3 Buddy D. Ratner	Asian- Pacific	Session 7 YasuhikoTabata	Session 11 Lorenzo Moroni		Session 15 Helen Lu
09:25|09:50			Daniel Cohn		Kelvin Yeung	Nuno Neves		Albino Martins
09:50|10:15			Devid Maniglio		Keiji Numata	Nesrin Hasirci		Patricia Diaz-Rodriguez
10:15|10:40			Horacio Cabral		Zhengwei Mao	Cristina Barrias		Julia Fernandez-Perez
10:40|11:05			Coffee-Break Poster Session 1		Coffee-Break Poster Session 2	Coffee-Break Poster Session 3		Coffee-Break
11:05|11:30			Session 4 Antonella Motta		Session 8 Nathaniel Hwang	Session 12 O9 & 010		Session 16 Tiago Silva
11:30|11:55			Carsten Werner		Leping Yan	O11 & O12		Closing Ceremony
11:55|12:20			Sei Kwang Hahn		Mitsuhiro Ebara	Manuel Salmeron Sanchez		
12:20|12:45			O1 & O2		Gilson Khang	Annalisa Tirella		
12:45|13:10		Lunch			Lunch	Lunch		
13:10|13:35								
13:35|14:00	Registration							
14:00|14:25	Opening Ceremony Session 1	Meet the Editor			Session 9 O5 & O6	Julio San Roman	Session 13 Andrés J. García	
14:25|14:50	Ehud Gazit				O7 & 08		Sanjukta Deb	
14:50|15:15	Helena Azevedo	Session 5 María Concepción Serrano		Giuseppe Battaglia			Pio González	
15:15|15:40	Gareth R. Williams	María J. Vicent		Michael Monaghan			Luis Diaz-Gomez	
15:40|16:05	Ana Paula Pêgo	Yu Shrike Zhang		Julianne Holloway			Thomas Groth	
16:05|16:30	Coffee-Break	Coffee-Break Poster Session 1		Coffee-Break Poster Session 2			Coffee-Break Poster Session 3	
	Session 2	Session 6		Session 10			Session 14	
16:30|16:55	Helena Tomás	O3 & O4		Miguel Alaminos			J. Carlos Rodríguez-Cabello	
16:55|17:20	Alicia El Haj	Miguel Oliveira		Shery Huang			Alejandro Sosnik	
17:20|17.45	Welcome Cocktail	Jai Prakash		Vamsi Yadavalli			Marcelo Calderón	
17:45|18:10		Vasif Hasirci		Loretta L. del Mercato			Luis Rojo	
18:10|18:35		Elizabeth Rosado Balmayor		Elżbieta Pamuła			Maria Rosa Aguilar	
20:00| ...						Dinner		

SCIENTIFIC PROGRAM

Day 1 | Monday 22nd	
13:35 | 14:00	**Registration**
14:00 | 14:25	**Welcome and Opening Ceremony** Rui L. Reis & Daniel Cohn *FBPS2025 Organizer & FBPS Founder*
Session 1 **Chair: Ricardo Pires**	
14:25 | 14:50	**Metabolite and peptide supramolecular polymers: from basic mechanisms to applications** Ehud Gazit *Tel Aviv University, Israel*
14:50 | 15:15	**Hyaluronan (HA): embracing this giant biopolymer to discover HA-based biomaterials with emergent properties** Helena S. Azevedo *i3S - University of Porto, Portugal*
15:15 | 15:40	**Developing "Phormulations" for Phages** Gareth R. Williams *UCL School of Pharmacy, UK*
15:40 | 16:05	**Rebuilding the Nervous System with Biomedical Polymers** Ana Paula Pêgo *i3S - University of Porto, Portugal*
16:05 | 16:30	**Coffee-Break**
Session 2 **Chair: Antonella Motta**	
16:30 | 16:55	**Dendrimers for Biomedical Applications** Helena Tomás *CQM- University of Madeira, Portugal*
16:55 | 17:20	**Engineering the stem cell niche using instructive and dynamic biomaterials** Alicia El Haj *University of Birmingham, UK*
17:20 | 18:35	**Welcome Cocktail**

Day 2 | Tuesday 23rd

	Session 3 **ALLAN HOFFMAN SESSION** **Chairs: Buddy Ratner & Daniel Cohn**
09:00 | 09:25	**The Legacy of Allan S. Hoffman and His Impact on My Thinking on Kidney Dialysis** Buddy Ratner *University of Washington, USA*
09:25 | 09:50	**3D printing: from the "ink" to the cardiac device** Daniel Cohn *The Hebrew University of Jerusalem, Israel*
09:50 | 10:15	**Engineering biopolymer-based nanotraps via molecular imprinting for target-specific sequestration** Devid Maniglio *University of Trento, Italy*
10:15 | 10:40	**Polymeric Nanomedicines for Targeted Cancer Immunotherapy** Horacio Cabral *University of Tokyo, Japan*
10:40 | 11:05	**Coffee-Break | Poster Session 1: Core Biomaterials, Nanomedicine & Tumor Models**
	Session 4 **ALLAN HOFFMAN SESSION** **Chairs: Buddy Ratner & Daniel Cohn**
11:05 | 11:30	**Silk-ink for human health: a versatile platform for precision biomaterials** Antonella Motta *University of Trento, Italy*
11:30 | 11:55	**Biohybrid and Fully Synthetic Polymer Hydrogels for Cell-Instructive Matrices** Carsten Werner *Leibniz Institute of Polymer Research Dresden, Germany*
11:55 | 12:20	**Smart Healthcare Materials and Devices for Theranostic Applications** Sei Kwang Hahn *Pohang University of Science and Technology, South Korea*
12:20 | 12:45	**01 - Multifunctional nanoparticles for tracking encephalitogenic cells in a multiple sclerosis model** Luis García-Fernández *Institute of Polymer Science and Technology, (ICTP), CSIC, Spain* **02 - Altered interaction between stem cells and collagen in an oxidative environment** George P. Altankov *Leonardo da Vinci Center of Competence in Personalized Medicine, 3D and Telemedicine, Robotic and Minimally Invasive Surgery, Bulgaria*
12:45 | 14:00	**Lunch**

12:45 | 14:00	Lunch
14:00 | 14:50	**Meet the Editor** Rui L. Reis & Jessica Wang *Ke Ai Publishing*
	Session 5 **Chair: Nuno Neves**
14:50 | 15:15	**Piezo4Spine: Novel strategies for neural repair after spinal cord injury** María Concepción Serrano *The Spanish National Research Council (CSIC), Spain*
15:15 | 15:40	**Polypeptide-Based Nanomedicines: Enhancing Tropism and Overcoming Biological Barriers** Maria J. Vicent *Prince Felipe Research Center, Spain*
15:40 | 16:05	**Unconventional additive (bio)manufacturing methods for regenerative medicine** Yu Shrike Zhang *Harvard Medical School, USA*
16:05 | 16:30	Coffee-Break | Poster Session 1: Core Biomaterials, Nanomedicine & Tumor Models
	Session 6 **Chair: Andrés J. García**
16:30 | 16:55	**O4 - Engineered microcarriers for enhanced spheroid-based regeneration of diffuse cartilage lesions** Desiré Venegas-Bustos *BIOFORGE Lab, University of Valladolid, Spain*
16:55 | 17:20	**Advances in biomaterials as artificial extracellular matrices in in vitro tumour models** Joaquim Miguel Oliveira *3B's Research Group, University of Minho, Portugal*
17:20 | 17:45	**Advanced 3D Bioengineered Tumor Models to Evaluate Targeted (Nano)Therapeutics** Jai Prakash *University of Twente, The Netherlands*
17:45 | 18:10	**The polymer heaven for biomedical applications** Vasif Hasirci *Acibadem University, Turkey*
18:10 | 18:35	**Taking mRNA Therapeutic Potentials to the Next Level: Enhancing Bone Regeneration through Rational RNA Combinations** Elizabeth Rosado Balmayor *RWTH Aachen University Hospital, Germany*

Day 3 | Wednesday 24th	
Session 7 **ASIAN-PACIFIC SESSION** **Chair: Gilson Khang**	
09:00 | 09:25	**Biomaterial-based tissue regeneration therapy based on natural self-healing potential and inflammation** Yasuhiko Tabata *Kyoto University, Japan*
09:25 | 09:50	**Enhancing Antibacterial Efficacy: Leveraging Stimuli-Responsive Mechanisms to Modulate Reactive Oxygen Species in Nanoparticle Design** Kelvin Yeung *The University of Hong Kong, Hong Kong SAR, China*
09:50 | 10:15	**Rational Polypeptide Design via Database Integration: Applications in Scaffolds and Mitochondrial Gene Delivery** Keiji Numata *Kyoto University, Japan*
10:15 | 10:40	**Nanozymes-armed microbes for disease treatment** Zhengwei Mao *Zhejiang University, China*
10:40 | 11:05	Coffee-Break | Poster Session 2: Hydrogels, Wound Healing & Regenerative Biology
Session 8 **ASIAN-PACIFIC SESSION** **Chair: Yasuhiko Tabata**	
11:05 | 11:30	**Biomaterials for immunoisolation and tissue adhesion, and anti-adhesive barriers** Nathaniel Hwang *Seoul National University, South Korea*
11:30 | 11:55	**Elastin-based hydrogels promote wound healing by regulating the tissue immune microenvironment** Leping Yan *The Seventh Affiliated Hospital of Sun Yat-sen University, China*
11:55 | 12:20	**Smart Polymer Technologies for Global Health** Mitsuhiro Ebara *Research Center for Macromolecules and Biomaterials, National Institute for Materials Science (NIMS), Japan*
12:20 | 12:45	**Development of Functional Scaffold Biomaterials and Bioactive Molecules from Natural Resources** Gilson Khang *Jeonbuk National University, South Korea*
12:45 | 14:00	Lunch

Session 9 Chair: Nathaniel Hwang	
14:00 | 14:25	**05 - Flexible and stretchable fet-type sensors based on organic and polymeric materials** Joon Hak Oh *Seoul National University, South Korea* **06 - Rationally designed h2o2 activatable antioxidant polymer nanoparticles for diagnosis and therapy of renal ischemia/reperfusion injury** Dongwon Lee Department of Bionanotechnology and Bioconvergence Engineering, *Jeonbuk National University, South Korea*
14:25 | 14:50	**07 - Understanding biophysical stimuli in three-dimensional microenvironments to enhance reprogramming efficiency toward induced pluripotency** Deogil Kim *Dongguk University Department of Biomedical Engineering, South Korea* **08 - 4D Biomimetic and multi-stimuli responsive interfaces for enhanced in vitro models and regenerative medicine** Silvia Panseri *Institute of Science, Technology and Sustainability for Ceramics (ISSMC), National Research Council of Italy, Italy*
14:50 | 15:15	**Beyond barrier crossing: nanomedicine as a therapeutic strategy for blood-brain barrier repair in dementia** Giuseppe Battaglia *Institute for Bioengineering of Catalonia (IBEC), Spain*
15:15 | 15:40	**Bioelectricity in Tissue Engineering: The role of electrical stimulation and electroconductive biomaterials in macrophage function and spinal cord therapeutics** Michael Monaghan *School of Engineering, Trinity College Dublin, Ireland*
15:40 | 16:05	**Design of magneto-responsive, fiber-hydrogel composites to enable three-dimensional spatial and temporal control over fiber alignment** Julianne Holloway *Arizona State University, USA*
16:05 | 16:30	Coffee-Break | Poster Session 2: Hydrogels, Wound Healing & Regenerative Biology

Session 10 Chair: Lorenzo Moroni	
16:30 | 16:55	**Generation and clinical translation of a fibrin-agarose bioengineered human cornea generated by tissue engineering** Miguel Alaminos *University of Granada, Spain*
16:55 | 17:20	**Electronic Spider Silk-Mimetics for Skin-Imperceptible Bioelectronics** Shery Huang *University of Cambridge, UK*
17:20 | 17:45	**Nature-derived, photo-actuated biomaterials for the fabrication of functional biodevices** Vamsi Yadavalli *Virginia Commonwealth University, USA*
17:45 | 18:10	**Multifunctional Platforms for Cell Sensing in Heterogeneous Systems** Loretta L. del Mercato *Nanotechnology Institute of National Research Council of Italy, Italy*
18:10 | 18:35	**Polymeric dry powder formulations of antibiotics and quorum sensing inhibitors for the treatment of lung infections** Elzbieta Pamuła *AGH University of Krakow, Poland*

Day 4 | Thursday 25th	
Session 11 **Chair: Vasif Hasirci**	
09:00 | 09:25	**Do cells like better rock music or classic music? A sonomechanobiology journey into orchestrating tissue regeneration** Lorenzo Moroni Maastricht University, MERLN Institute for Technology, The Netherlands
09:25 | 09:50	**Functionalized substrates and nanostructures for advanced therapies** Nuno M. Neves *3B's Research Group, University of Minho, Portugal*
09:50 | 10:15	**Smart polymers: towards future applications** Nesrin Hasirci *Middle East Technical University (METU), Chemistry Department, Turkey*
10:15 | 10:40	**Engineering Vascularized Stroma for In Vitro Modeling of Human Tissues and Disease** Cristina C. Barrias *i3S – University of Porto, Portugal*
10:40 | 11:05	**Coffee-Break | Poster Session 3: Advanced 3D Bioprinting & Marine/Sustainable Biomaterials**
Session 12 **Chair: Cristina Barrias**	
11:05 | 11:30	**O9 - Glycopeptide-based hydrogels as storage depots that promote vascularization** Ana Rita Araújo *3B's Research Group, University of Minho, Portugal* **O10 - Bioengineered microtissue constructs for dual osteogenic and angiogenic stimulation to restore bone integrity in osteoradionecrosis** Christiane L. Salgado *i3S – University of Porto, Portugal*
11:30 | 11:55	**O11 - Toward microbiome models: bacteria encapsulation in interfacial polyelectrolyte complexes** Rui R. Costa *3B's Research Group, University of Minho, Portugal* **O12 - Engineering regenerative niches:Encapsulation of stromal cells from iPSC-derived intestinal organoids in synthetic degradable microgels** Ana Mora-Boza *University of Galway, Ireland*
11:55 | 12:20	**Engineered biomaterials for regeneration and mechanobiology** Manuel Salmeron Sanchez *Institute for Bioengineering of Catalonia, IBEC, Spain*
12:20 | 12:45	**Manufacturing of Natural-Based Nano-in-Micro Hydrogels for Controlled Site Specific Delivery of Therapeutic Agents** Annalisa Tirella *University of Trento, Italy*

12:45 | 14:00	Lunch
	Session 13 JULIO SAN ROMAN SESSION Chairs: Maria Rosa Aguilar & Luis Rojo
14:00 | 14:25	**Bioengineered Hydrogels for Regenerative Medicine** Andrés J. García *Georgia Institute of Technology, USA*
14:25 | 14:50	**Stimulating Bone Regeneration and Vascularisation: Poly(Vinyl Alcohol) Hydrogel-mineral composites** Sanjukta Deb *King's College London, UK*
14:50 | 15:15	**Engineering of in vitro 3d bone tissue models via bioprinting technologies** Pio González *CINTECX, University of Vigo, Spain*
15:15 | 15:40	**Engineering cell-instructive 3D scaffolds via laser surface microstructuring** Luís Diaz-Gomez *University of Santiago Compostela, Spain*
15:40 | 16:05	**Ternary Multilayer Systems for Programming Cell Behaviour** Thomas Groth *Martin Luther University Halle-Wittenberg, Germany*
16:05 | 16:30	Coffee-Break | Poster Session 3: Advanced 3D Bioprinting & Marine/Sustainable Biomaterials
	Session 14 JULIO SAN ROMAN SESSION Chairs: Maria Rosa Aguilar & Luis Rojo
16:30 | 16:55	**Engineering Complex Coacervation to Obtain Functional Biomolecular Condensates Through Recombinant Polypeptides** José Carlos Rodríguez-Cabello *University of Valladolid, Bioforge Lab, LaDIS, CIBER-BBN, Spain*
16:55 | 17:20	**Self-assembled nano-drug delivery systems** Alejandro Sosnik *Israel Institute of Technology, Haifa, Israel*
17:20 | 17:45	**Multiresponsive polymer nanoparticles for mucosal drug delivery** Marcelo Calderón *POLYMAT, Applied Chemistry Department, Faculty of Chemistry, University of the Basque Country (UPV/EHU), Spain*
17:45 | 18:10	**Innovative hydrogel platforms for controlled release in regenerative medicine** Luis Rojo *Institute of Polymer Science and Technology, (ICTP), CSIC, Spain*
18:10 | 18:35	**Biomaterials at the frontier of biomedical innovation: a legacy of scientific excellence and translational impact** Maria Rosa Aguilar *Institute of Polymer Science and Technology, (ICTP), CSIC, Spain*
20:00	Conference Dinner

Day 5 | Friday 26th	
Session 15 **Chair: Miguel Oliveira**	
09:00 | 09:25	**To be annouced** Helen Lu Columbia University, USA
09:25 | 09:50	**Biofunctional nanostructured biomaterials aiming target therapies** Albino Martins *3B's Research Group, University of Minho, Portugal*
09:50 | 10:15	**Polymeric and lipid-polymer drug delivery systems for cell-specific modulation in musculoskeletal disorders** Patricia Diaz-Rodriguez *University of Santiago de Compostela, Spain*
10:15 | 10:40	**Exploring light-based biofabrication of norbornene-functionalized polymers for recreation of cell microenvironments** Julia Fernández Pérez *TU Wien, Austria*
10:40 | 11:05	**Coffee-Break**
Session 16 **Chair: José Carlos Rodríguez-Cabello**	
11:05 | 11:30	**Marine-origin biopolymers as constitutive elements of biomaterials: a blue biotechnology contribution to advanced therapies** Tiago H. Silva *3B's Research Group, University of Minho, Portugal*
11:30 | 11:55	**Closing Ceremony** Rui L. Reis & Daniel Cohn *FBPS2025 Organizer & FBPS Founder*

POSTER LIST

Poster Session 1 | Tuesday 23rd Core Biomaterials, Nanomedicine & Tumor Models		
Nº. Poster	**Presenting Author**	**Title**
1	H.-C. Yang	Immunomodulatory activity of polycaprolactone nanofibers grafted with phosphatidylserine and arginine-glycine-aspartic acid (RGD)
2	V. M. Nogueira	Sequential extraction of collagen and gelatin from the skins of codfish, meagre and blue shark in the perspective of application in healthcare
3	K. K. Sub	Bile acid-conjugated nanoparticles for enhanced gastrointestinal absorption
4	A. Jobdeedamrong	Polyplex-based co-delivery of paclitaxel and MIR-34a for advancing combination therapy in colorectal cancer
5	J. Moon	Photo-crosslinked biodegradable adhesives inspired by diphenol crosslinking in resilin proteins
6	R. Lima-Sousa	The rise of in vitro models in investigating tumor-induced cachexia
7	H. Ferreira	A multifunctional hydrogel to damage residual glioblastoma cells post-resection
8	L. M. Sousa	Exploring biomaterials for pelvic organ prolapse repair: biocompatibility performance
9	R. Komsa Penkova	Unravelling the effects of glycated collagen on MSC adhesion and mechanotransduction
10	B. L. Correia	Lighting up the tumor microenvironment: engineering biomedical polymer optics for next-generation living optical fibers
11	D. K. Lee	Targeted restoration of tumor suppressor function of pten via systemic nanocomplex-mediated gene delivery
12	L. M. Topalova	Harnessing the paracrine power of MSCs: enhancing adipose stem cell regenerative traits using exogenous secretome
13	D. Peixoto	Antibacterial nanoparticles based on chitosan/methacrylated hyaluronic acid for treatment of chronic wounds
14	K. Na	A light-activated antibody-polymer system for targeted cytotoxicity and immune stimulation in resistant cancers
15	A. R. Franco	Bioengineered viscoelastic spider silk-based bilayer patch for abdominal tissue regeneration
16	T. H. Silva	Effect of extraction conditions on the composition and bioactivity of brown seaweeds extracts
17	C. H. Kim	Targeting of hyaluronic acid based nanoparticles in 3d tumor spheroid and micro-fluidic model

Nº. Poster	Presenting Author	Title
18	F. Branco	Click-to-print 3d gummies: a layered nanostructured lipid carrier platform for pediatric brain tumor treatment
19	S. Mark	Engineering reverse thermo-responsive nanoshells
20	K. Kim	Pulmonary surfactant-mimetic inhalable nanoparticles for targeted drug delivery and immunomodulation in lung cancer
21	W. Hao	Hepatocellular carcinoma-targeted drug delivery hydrogel based on boronate ester bond stability modulation
22	Z. Peselev	Engineering in situ weldable vascular devices
23	K.S. Kim	Synthesis of sitosterol-doxorubicin derivatives and preparation of nanoparticles for anticancer therapy
24	N. Park	Choline-decorated polymeric nanoparticles for synergistic anticancer efficacy through enhanced drug delivery and phospholipid synthesis inhibition
25	H. J. Choi	Highly sensitive mechanochromic biomedical sensor capable of identifying cancer cells' metastatic tendency
26	K. L. O'Neill	Melt electrowriting polymers for scaffold fabrication
27	V. M. Correlo	Cytotoxicity evaluation of a miniaturized flexible oxygen biosensor
28	D. Caballero	Human microcirculation-on-a-chip model reveals lung cancer-driven lymphatic remodeling and invasion

Poster Session 2 | Wednesday 24th Hydrogels, Wound Healing & Regenerative Biology		
Nº. Poster	**Presenting Author**	**Title**
29	D. A. Domingo-Lopez	Thioketal-biopolymer systems as a platform for ros-responsive drug delivery and regenerative applications
30	S. Gimondi	Decellularized kidney extracellular matrix: a tunable biopolymer for renal repair
31	C. F. Guimarães	Microfluidic manipulation of biomedical polymers for the biofabrication of miniaturized 3D cancer architectures
32	F. R. Maia	Electroactive nanocomposite hydrogels for bone repair: integration of nanohydroxyapatite-decorated carbon nanotubes
33	M. R. Casanova	A biomimetic microfluidic strategy for efficient tumor cell isolation using electrospun membranes
34	M. S. Orellano	Incorporation of acidic monomers into responsive nanogels modulates antimicrobial release and enhances penetration into bovine udder tissue
35	D. Soares da Costa	Biomimetic blood-brain barrier model engineered via cell sheet technology and microfluidics
36	K. J. Lee	Adhesive and hemostatic microneedles based on biomaterials
37	I. B. Leonor	Engineered injectable antibacterial spider silk-alginate hydrogels for veterinary wound healing
38	Y.-J. Kim	Bioactive magnesium-collagen/ha hydrogel crosslinked by visible light for infected wound healing
39	T. Z. Stoyanova	Bioactive plcl nanofibers for enhanced wound healing
40	L. P. da Silva	Tuning macrophages responses with fibroblasts-derived extracellular matrix
41	L. P. da Silva	Exploring the immunogenecity of gellan gum-based inks for 3D bioprinting of human macrophage-integrating human tissues
42	S. J. Park	Multifunctional collagen and cellulose nanofiber mat containing peptide drug for hemostasis and skin repair
43	I. Vilela de Sousa	A self-healing alginate hydrogel enriched with ECM cues to promote vascularization and skeletal muscle regeneration
44	S. Panseri	3D in vitro models of osteosarcoma: a novel hydrogel-scaffold system for therapeutic research
45	H. A. Kim	Injectable and degradable oxidized alginate hydrogels incorporating PANI:PSS nanoparticles for advanced photothermal therapy

No. Poster	Presenting Author	Title
46	M. T. Rodrigues	Investigating bioengineered spider silk sutures - from antibacterial properties to immune dynamics
47	K. M. Huh	Preparation and evaluation of a novel dual-crosslinkable hybrid thermogel for tissue engineering
48	M. Parmaksiz	Decellularized tendon-based injectable regenerative hydrogels: optimization of decellularization protocols and cross-species comparative analyses
49	N. S. Parmaksiz	Development and characterization of decellularized bone tissue-based bioadhesive regenerative hydrogel
50	C. Correia	Dopamine-functionalized hyaluronic acid hydrogels for anti-inflammatory delivery in neural tissue applications
51	A. C. Amaral	Impact of the addition of beta tricalcium phosphate (β-TCP) on the micro/nanotopography and cytocompatibility of poly(lactic-co-glycolic acid - PLGA) scaffolds for application in bone regenerative medicine
52	K. So	Development of decellularized urinary bladder matrix based cryogel for promoting angiogenesis.
53	V. I. B. Castro	Self-assembling GHK-based peptides: enhanced proteolytic stability for accelerated wound repair
54	I. S. Raja	Enhanced tissue regeneration potential of the combinatorial treatment of photobiomodulation and nanofiber mat in skin wound healing
55	S. Gujjar	Human placental ecm hydrogels: a bioactive scaffold for regenerative medicine
56	H. Shin	Modulating hydrogel properties through silk fibroin hydrolysis: a strategy for tissue engineering scaffolds
57	S-N. Jang	Mechanically reinforced gellan gum hydrogel designed as a carrier for corneal endothelial cell transplantation
58	S. Freitas-Ribeiro	Impact of preservation techniques on the extracellular matrix of cell sheet constructs

Poster Session 3 | Thursday 25th Advanced 3D Bioprinting & Marine/Sustainable Biomaterials		
Nº. Poster	**Presenting Author**	**Title**
59	Y. Park	Applying torque to the cell membrane using magnetic stimulation system enhance the functinoal maturation of cardiac organoids
60	I. F. Cengiz	Pressure-responsive conductive gelatin-alkali lignin hydrogels developed for meniscus repair
61	S. Pina	3D printing of brushite-forming cu-substituted β-TCP cements for bone tissue engineering
62	D. E. Beyza	3D printed PDRN/GELMA bioink for muscle tissue engineering
63	D. B. Rodrigues	Engineering a 3D hydrogel model to study tumor–stromal cell communication
64	C. R. Casanova	Engineering a biomimetic intestinal scaffold with tunable villi architecture via dlp 3D printing
65	J. Silva-Correia	Gelatin-based and gellan gum-based bioinks for 3D (bio)printing of composite structures
66	L. C. Rodrigues	Freeze-dried polysaccharide-based tubular constructs with enhanced biofunctionality via recombinant polypeptides
67	S. Pionato	Cross-linked elr hydrogel containing an embedded thermoresponsive coacervate that decouples elasticity from viscous relaxation for stem-cell mechanoregulation
68	L. C. Costa	From cytotoxic to cytocompatible: tailoring PLA/ZNO scaffolds via silane functionalization
69	S. Pérez-Davila	GELMA derived from fish by-products for 3D bioprinting
70	R. P. Pirraco	Extracellular matrix-based hydrogels from stromal vascular fraction cell sheets to support vascular network formation
71	A. Perioli	Micropatterned glycopeptide-based hydrogels that promote cellular alignment for cardiac repair
72	I. Pashkuleva	Biocatalytic-induced supramolecular chirality in carbohydrate-based systems
73	T. H. Silva	Sustainable drug delivery platforms based on starfish-derived biphasic calcium phosphate
74	A. B. Sousa	Fibrin-based immunomodulatory hydrogels incorporating maresin-1–loaded zein nanoparticles for enhanced wound healing
75	F. C. M. Lobo	Forest biomass-derived biopolymers for enhancing antioxidant, flexibility, and antibacterial activity of poly(lactic acid) films targeting safer applications
76	R. O. Sousa	Supercritical co_2 decellularization of codfish skin for ECM-based biomaterials

Nº. Poster	Presenting Author	Title
77	A. Gomes	Modified gellan gum nanoparticles as drug delivery vehicles
78	M. García-Gonzalez	Marine-based injectable platforms: development of cryogels for cartilage repair using fish collagen, chondroitin sulfate and hyaluronic acid
79	A. C. Amaral	Functionalization of PLGA/β-TCP scaffolds with silk fibroin for application in bone regenerative medicine: a topographic analysis
80	P. E. A. Gaspar	Rheological influence of meniscus-derived decellularized extracellular matrix on hyaluronic acid hydrogels for biomedical applications
81	M. S. Rocha	Biomedical potential of chondrosia reniformis collagen for scaffold development in tissue engineering
82	M. V. Magalhães	Engineering a vascularized 3D model of the spleen red pulp
83	M. Y. Ha	Therapeutic potential of bioactive glass nanoparticles in spinal bone regeneration
84	M. Y. Ha	Osteoinductive bioactive glass–poly (mMPC-co-Butyl methacrylate) composites for mandibular bone regeneration
85	N. Kim	Injectable TGF-β3-loaded hyaluronic acid hydrogel enhances cartilage regeneration via controlled release and microfracture-induced stem cell recruitment

HONOR SPECIAL SESSIONS

This meeting will commemorate our 30th years of organizing this very successful meeting. In addition to honour the founders of the FBPS meeting we will have two special sessions to honour the recently deceased Prof. Julio San Roman and Prof. Allan Hoffman. Allan was one of the most supportive members in the biomaterial's community and an inspiration for many years for all of us working on biomedical polymers. Julio was one of the most active members of FBPS and one of the committee members, having organized FBPS both in Granada and in Tenerife.

Professor Allan S. Hoffman's Biographical Summary

Professor Allan S. Hoffman (October 27, 1932 – December 15, 2023) was a pioneering bioengineer and chemical engineer whose work had profound impact on biomaterials, drug delivery, and smart polymers.

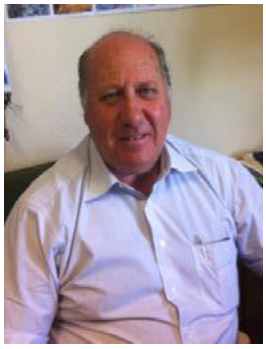
He joined the University of Washington (UW) in 1970, initially in Chemical Engineering, and played a key role in the establishment of the UW Center for Bioengineering, which later became the Department of Bioengineering in 1997.

Professor Hoffman's scientific contributions include the development and application of temperature- and pH-responsive "intelligent" polymers and hydrogels, innovations in biomaterial surface design (non-fouling and bioactive surfaces), and extensive work in controlled drug delivery and diagnostics. He introduced polyNIPAM for biomedical applications.

Over his career, he published over 500 research papers. He was inventor in hundreds of granted patent applications of which many were licensed, thus bridging fundamental science with translational and commercial applications.

Professor Hoffman was widely recognized internationally: in 2005 he was elected to the U.S. National Academy of Engineering (NAE); he received multiple prestigious awards including the Acta Biomaterialia Gold Medal (2017), the Founders Awards of the Society for Polymer Science (Japan) and the Controlled Release Society Foundation Award (2016); and in 2015 he was named among Thomson Reuters' "World's Most Influential Scientific Minds." Based on the citations to his publications.

Allan Hoffman traveled the world as an "ambassador for biomaterials," educating others on the importance and unique challenges of biomaterials in medicine and biology. Beyond his research, he was a beloved mentor of graduate students and post-doctoral researchers, known for his warmth, generosity, and commitment to advancing the field through education and collaboration.



Professor Julio San Roman's Biographical Summary

Professor Julio San Román (November 15, 1949 - September 20, 2023) was a distinguished researcher in the field of biomaterials and polymer science, with a long-standing career characterised by innovation, leadership, and interdisciplinary impact.

He got a Doctorate in Chemistry (Polymer Science), awarded in 1975, and led for many years the Biomaterials Group at the Instituto de Ciencia y Tecnología de Polímeros (ICTP), Consejo Superior de Investigaciones Científicas (CSIC), Madrid. He was a major partner of the EXPERTISSUES network of excellence on tissue engineering and regenerative medicine.

Over more than four decades, Professor San Román has made foundational contributions to the design, synthesis, and application of polymer-based systems for biomedical use, especially in tissue engineering, controlled drug delivery, bioactive hydrogels, biopolymer-drugs, and functional polymer coatings.

He has held major leadership roles in professional societies, including serving as President of the Iberian Society for Biomechanics and Biomaterials, of the Polymer Section of the Spanish Royal Society of Chemistry, and of the European Polymer Federation. He was a long-standing member of the European Society for Biomaterials (ESB), served on its Council, and helped organise key international congresses in the field, including ESB annual meetings and for two times the FBPS symposium.

His publication record is extensive: over 400 peer-reviewed scientific articles in journals spanning polymer science, biomaterials, and biomedical applications; many book chapters; and editorial contributions, as well as more than 25 granted patents. His work not only advanced basic understanding but has a strong translational dimension, including industrial collaborations and interest in medical device applications. We received several major international awards, including the George Winter from ESB in 2018.

Professor San Román's influence also extends through mentorship of graduate students and researchers, international cooperation (including in Latin America and the Caribbean), and sustained involvement in projects that address health, regeneration, and the development of novel therapeutic materials.

KEYNOTE LECTURES - Session 1

Metabolite and peptide supramolecular polymers: from basic mechanisms to applications

Ehud Gazit[1,2,3]

[1]The Shmunis School of Biomedicine and Cancer Research, Faculty of Life Sciences, Tel Aviv University;[2]Department of Materials Science and Engineering, Faculty of Engineering, Tel Aviv University;[3]Sagol School of Neuroscience, Tel Aviv University

The spontaneous self-assembly of small biological molecules into ordered supramolecular structures represents a fundamental principle of molecular organization with broad implications across the physical and life sciences. We systematically investigated the supramolecular polymerization of peptides, metabolites, and their hybrid assemblies, elucidating the physicochemical mechanisms that govern their formation. Employing a reductionist strategy, we demonstrated that minimalistic building blocks—including dipeptides, tripeptides, and small-molecule metabolites—can give rise to diverse architectures such as crystalline fibrils, helical-like ribbons, and amorphous glassy materials. The assembly processes are driven by a combination of hydrogen bonding, aromatic interactions, and the mediation of structural water or metal coordination, resulting in systems with distinct mechanical, optical, and catalytic properties. Beyond providing mechanistic insights into self-organization phenomena, this research establishes a foundation for the development of functional supramolecular materials. We highlight applications spanning biocompatible adhesives, piezoelectric nanodevices, environmental bionanozymes, and optoelectronic materials, culminating in the discovery of self-healing, transparent peptide glasses with broad spectral transmission and high mechanical robustness. These findings position metabolite and peptide supramolecular polymers as a versatile and sustainable class of biomolecular materials, offering new opportunities for technological innovation at the interface of chemistry, biology, and engineering.

Selected References: 1. Finkelstein-Zuta, G., Arnon, Z.A., Vijayakanth, T., Messer, O., Lusky, O.S., Wagner, A., Zilberman, G., Aizen, R., Michaeli, L., Rencus-Lazar, S. Gilead, S., Shankar, S., Pavan, M.J., Goldstein, D.A., Kutchinsky, S., Ellenbogen, T., Palmer, B.A., Goldbourt, A., Sokol, M. & Gazit E. (2024) A Self-healing Multispectral Transparent Adhesive Peptide Glass. Nature 630, 368-374. 2. Makam, P., Yamijala, S.S.R.K.C., Tao, K., Shimon, L. J. W., Eisenberg, D. S., Sawaya, M. R., Wong, B. M. & Gazit, E. (2019) Non-proteinaceous Hydrolase Comprised of Phenylalanine Metallosupramolecular Amyloid-Like Structure. Nature Catal. 2, 977–985. 3. Chakraborty, P., Tang, Y., Yamamoto, T., Yao, Y., Guterman, T., Zilberzwige-Tal, S., Adadi, N., Ji, W., Dvir, T., Ramamoorthy, A., Wei, G. & Gazit, E. (2020) Unusual Two-Step Assembly of a Minimalistic Dipeptide-Based Functional Hypergelator. Adv. Mater. 32, e1906043. 4. Bera, S., Mondal, S., Xue, B., Shimon, L. J. W., Cao, Y. & Gazit, E. (2019) Rigid Helical-Like Assemblies from a Self-Aggregating Tripeptide. Nature Mater. 18, 503-509. 5. Tao, K., Makam, P., Aizen, R. & Gazit, E. (2017) Self-Assembling Peptide Semiconductors. Science 358, eaam9756. 6. Berger, O., Adler-Abramovich, L., ... & Gazit, E. (2015) Light-Emitting Self-Assembled Peptide Nucleic Acids Exhibit Both Stacking Interactions and Watson-Crick Base Pairing. Nature Nanotech. 10, 353-360.

Hyaluronan (HA): embracing this giant biopolymer to discover HA-based biomaterials with emergent properties

Helena S. Azevedo

i3S – Instituto de Investigacao e Inovacao em Saude, Universidade do Porto, Portugal
INEB – Instituto de Engenharia Biomedica, Universidade do Porto, Portugal

Hyaluronan (HA) is a unique, highly abundant, extracellular matrix (ECM) polysaccharide found throughout mammalian connective tissues. Its biomedical utility stems from its many attributes, such as biodegradability, biocompatibility, polyanionic charge, elastoviscous behaviour and ease of chemical modification (Fig. 1).

Fig. 1: Key physicochemical and biological properties of HA (taken from [1]).

In this talk, I'll be sharing the versatility of HA biopolymer for preparing hydrogels for the delivery of molecular and cellular therapies [1, 2], with particular emphasis on the supramolecular crosslinking of native HA with amphipathic cationic peptides [3].

References: [1] J. Silva, H. S. Azevedo, Bioengineered Hyaluronan Hydrogels for the Delivery of Molecular and Cellular Therapies. Adv. Therap. 2023, 7, 2300182.
[2] L. Wu, S. D. Cio, H. S. Azevedo, J. E. Gautrot, Photoconfigurable, Cell-Remodelable Disulfide Cross-linked Hyaluronic Acid Hydrogels, Biomacromolecules 2020, 21, 4663.
[3] Y. Yuan, Y. Shi, J. Banerjee, A. Sadeghpour, H. S. Azevedo, Structuring Supramolecular Hyaluronan Hydrogels via Peptide Self-assembly for Modulating the Cell Microenvironment, Mater. Today Bio. 2023, 19, 100598.

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Developing “Phormulations” for Phages

Sai Liu,[1] Tian Ju,[1] Jixuan Li,[1] Andrew Weston,[1] Giovanni Satta,[2] Sara Bolognini,[3] Mariagrazia Di Luca,[3] Simon Gaisford,[1] Gareth R. Williams[1]

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Bacterial infections contribute to millions of deaths (7.7M in 2019). The most common medical intervention to combat these is the use of antibiotics. However, the emergence of multi-drug-resistant bacteria is a significant and growing threat associated with ca. 4.95M deaths in 2019 [1]. Pseudomonas aeruginosa (P. aeruginosa) is a particularly problematic bacterial pathogen, commonly seen in e.g. wounds and lung infections. Bacteriophages, or phages, are viruses which infect bacteria. They are highly specific to particular strains of bacteria, and can be used safely without the risk of off-target effects on e.g. the gut microbiome. Phages offer a natural alternative to antibiotics, and are self-amplifying and adaptable. They are thus capable of circumventing bacterial resistance.

The clinical efficacy of phages is well established. However, most studies prepare phages as simple liquid suspensions: this causes challenges with transport and stability, and there is a pressing need to develop solid phage formulations. In this presentation, we will discuss recent work to develop such formulations using electrohydrodynamic atomization (EHDA; electrospinning and electrospraying). EHDA applies electrical energy to dry a polymer/active component solution, offering a number of advantages over more conventional approaches such as spray drying and freeze drying in terms of simplicity and the lack of heat application.

Anti-P. aeruginosa Neko phages were isolated from puddle water. They were first characterized and then processed into fibers by electrospinning and particles by electrospinning, using polymer and sugar excipients. The resultant products were characterized for their morphology (electron microscopy), phage content, and effectiveness in anti-bacterial assays. The phage-loaded fibers are found to be cylindrical and smooth [2], while regular spherical particles of ca. 1-2 μm in diameter can be generated by electrospraying [3]. We find a loss of phage activity after EHDA processing, but this can be minimized by careful optimization of the formulation. The optimal phage formulations can effectively delay or prevent bacterial growth, with no reduction in activity compared to “fresh” phages. Furthermore, preparing systems where phages are combined with antibiotics allows for synergistic effects. We thus conclude that EHDA approaches have great potential for the development of solid phage formulations.

References: [1] Murray C J L, et al. Global burden of bacterial antimicrobial resistance in 2019: A systematic analysis. Lancet, 2022, 399(10325): 629-655.[2] Ju T, Li J, et al. Anti-Pseudomonas aeruginosa bacteriophage loaded electrospun fibers for antibacterial wound dressings. Macromol. Rapid Commun. 2025: 2400744.[3] Liu S, et al. Anti-Pseudomonas aeruginosa phage-loaded electrosprayed lactose particles. J. Drug Del. Sci. Technol. 2025, 107:106851.

Rebuilding the Nervous System with Biomedical Polymers

Ana Paula Pêgo

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INEB - Instituto de Engenharia Biomédica
ICBAS – Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto
Porto, Portugal

One of the major challenges in the field of neuroscience is developing effective therapies that enhance the regenerative capacity of the nervous system, leveraging advancements in basic research.
Our group leverages biomedical polymers both to dissect nervous system function in health and disease and to design strategies that promote tissue repair and regeneration.
In this talk, I will highlight how we have been using bioengineering to create macroglia tissue models for uncovering novel mechanobiology mechanisms and identifying new therapeutic targets. I will also discuss our work on biomaterial-based nanoparticles for targeted nucleic acid delivery to neurons, aimed at promoting neuroprotection and neuroregeneration. Special emphasis will be placed on innovative methodologies to evaluate these nanosystems and guide the design of more efficient therapeutics.

KEYNOTE LECTURES - Session 2

Dendrimers for Biomedical Applications

Helena Tomás

CQM-Centro de Química da Madeira, MMRG, Universidade da Madeira, Campus da Penteada, 9020-105 Funchal, Portugal

Dendritic polymers, including dendrimers, have attracted considerable interest in the biomedical field due to their high density of functional groups (multivalency), and customizable properties [1]. Depending on their composition, dendritic polymers can also be degradable, resulting in non-toxic products that are either excreted or metabolized without harmful effects to our body. Furthermore, hybrid materials incorporating dendritic polymers can be engineered to combine the distinct advantages of their components, leading to optimized systems with enhanced performance.
The aim of this lecture is to highlight several strategies under development at CQM for creating biomaterials based on dendrimers/dendritic polymers, namely: (a) nanoscale drug delivery platforms made from degradable bis-MPA (2,2-bis-(hydroxymethyl)propionic acid) dendrimers, either surface-functionalized [2] or integrated with fucoidan, a natural bioactive polysaccharide; (b) hydrogels formed from dendritic-linear-dendritic polymers corresponding to a linear polyethylene glycol (PEG) core flanked by bis-MPA-based dendrons; (c) thin films combining poly(amidoamine) dendrimers and dsDNA that are water-insoluble, highly elastic when air-dried, exceptionally stable over time, cytocompatible, and easily scalable [3].

References: 1. Tomás H., Rodrigues J. Dendrimers and Dendrimer-based Nano-objects for Oncology Applications in New Trends in Smart Nanostructured Biomaterials in Health Sciences, Materials Today Series (ed. G. Gonçalves, P. Marques, J. Mano), Elsevier Science, 2022. 2. Gonçalves M., Kairys V., Rodrigues J., Tomás H. Polyester dendrimers based on bis-MPA for doxorubicin delivery. Biomacromolecules, 2022, 23, 20-33. 3. Castro R., Granja P.L., Rodrigues J., Pêgo A.P., Tomás H. Bioinspired hybrid DNA/dendrimer-based films with supramolecular chirality, J. Mater.Chem. B, 2025, 13, 4671-4680.

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Engineering the stem cell niche using instructive and dynamic biomaterials

Alicia El Haj

Healthcare Technology Institute, Institute of Translational Medicine, University of Birmingham UK

Regenerative medicine principles are based on the ability of cells to regenerate and grow tissues in vitro and in vivo. Novel biomaterials and nanotechnology approaches combined with instructive cues enable the manufacture and control of cells used for regenerative models and clinical therapy. The interaction of biological factors such as the Wnt family of proteins combined with physical factors play a key role in providing a stem cell niche capable of rebuilding tissue complexity both in vitro and in vivo. Bio-magnetic nano-control systems can define differentiation of multiple cell types. This presentation will cover my lab's innovative advances in the field of instructive biomaterials and engineering tissues for the clinic. I will demonstrate how multidisciplinary teams within the Institute of Translational Medicine at Birmingham combine efforts to tackle these questions to translate Advanced therapies to the clinic.

References:

Okuchi et al 2021 Wnt-modified materials mediate asymmetric stem cell division to direct human osteogenic tissue formation for bone repair Nature Materials 20(1) 108-118 doi: 10.1038/s41563-020-0786-5

Markides et al (2018) Translation of remote control regenerative technologies for bone repair Npj Regenerative Medicine 3(9) doi.org/10.1038/s41536-018-0048-1

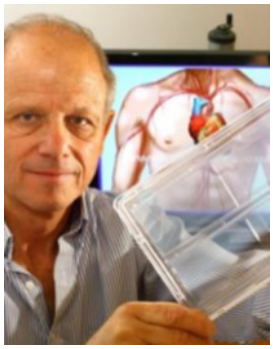
ALLAN HOFFMAN SESSION

The Legacy of Allan S. Hoffman and His Impact on My Thinking on Kidney Dialysis

Buddy Ratner

Departments of Bioengineering and Chemical Engineering, University of Washington, Seattle WA 98195 USA

In 1970, a lecture by Professor Allan S. Hoffman inspired me to focus on biomaterials and to travel to Seattle to work in his laboratory. Our focus then was blood compatibility of medical devices. The lessons learned, on both blood compatibility and participation in the academic community have served me well for 50+ years. In 1962, 10 years before my arrival in Seattle, the first human was saved from end stage kidney disease (ESKD) at the University of Washington by an amazing new technology, chronic hemodialysis. This talk reflects the teachings of Allan Hoffman and how they have impacted our recent developments. We are now (as we did 50 years ago) focusing on innovative bioengineering technology and on getting such improved technology expeditiously to patients to address significant human health issues. The 1962 hemodialysis technology developed in Seattle evolved to 4.5 million people worldwide receiving life-prolonging dialysis treatments three times a week. The therapy sustains the lives of kidney disease patients. However, the pain and complications of today's kidney dialysis are tragic for ESKD patients and the costs to society are huge (>$130B/yr). Our research program at the University of Washington is now focused on rethinking dialysis technology that has not changed significantly since 1962. We aim to develop an ambulatory dialysis system, the AKTIV (Ambulatory Kidney to Improve Vitality). To retool dialysis, we will need improved blood waste cleansing, painless blood access, new blood compatible materials, skin healing and prevention of biofilm formation. Enhancements that revolutionize how dialysis is performed will be discussed in this talk along with efforts to take innovation from the lab bench to the patient. Team science (i.e., The University of Washington Center for Dialysis Innovation, still another lesson learned from Professor Hoffman), has been instrumental in making this happen. Biomaterials feature significantly in our development effort and are used to improve blood compatibility, reduce biofilm formation and improve skin healing.



3D Printing: From the "Ink" to the cardiac device

Daniel Cohn

The Hebrew University of Jerusalem

The remarkable progress made in the 3D printing field in recent years has made possible the engineering of a myriad of new objects, including a diversity of medical devices. Nevertheless, only a new generation of 3D printed constructs, combining pioneering concepts and novel tailor-made materials ("inks"), will permit further progress. The ability to engineer custom-made medical devices and to implant them following minimally invasive procedures are two important trends in modern surgery. The personalization of the device is achieved by 3D printing it, while the capacity to deploy it minimally invasively harnesses the shape memory behavior displayed by the inks used. Heart failure, which holds a high mortality rate, remains one of the major public health problems worldwide. Myocardial remodeling and dilatation following myocardial infarction triggers a life-threatening process leading to heart failure. This talk introduces a 3D printed personalized cardiac restraint device (CARD) aimed at preventing cardiac remodeling and heart failure. The personalization of the CARD was achieved by 3D printing it, based on the precise digital information provided by the CT scan of the patient's failing heart. Most existing inks, which constitute the basic building blocks of the device, are typically stiff materials, clearly inappropriate for soft tissue applications, such as a CARD. In light of the above, new inks able to photo-crosslink under UV radiation during the printing process, were synthesized and analyzed. These new inks attained strength levels exceeding the clinical requirements, displaying also tunable low modulus and significant elongation at break values. The new inks differ in their composition, morphology and mechanical properties, allowing the optimal design of custom-made CARDs. This contribution will briefly describe the design of the flexible inks required for 3D printing the CARD, followed by studies conducted on rat and swine MI models. It was demonstrated that the CARD did not induce any maladaptive changes in the heart. Improved hemodynamic profiles following CARD implantation suggest enhanced left ventricular function and better fluid dynamics within both cardiac and pulmonary systems. Moreover, proper functioning of the CARD upon removal after 28 days was confirmed. Blood tests showed elevated lactate dehydrogenase and troponin levels following LAD ligation, that returned to baseline after implantation of the CARD.

Engineering biopolymer-based nanotraps via molecular imprinting for target-specific sequestration

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Recent advances in supramolecular engineering have opened new avenues for creating bioinspired metamaterials capable of selective molecular recognition. We present a pioneering approach that merges tissue engineering, polymer chemistry, and molecular imprinting technology (MIP) to develop biopolymer-based, multifunctional metamaterials—termed bioMIPs—with intrinsic molecule-scavenging properties. These nanostructured materials are produced using biocompatible, clinically relevant proteins such as methacrylated Silk Fibroin (SilMA) and Gelatin Methacryloyl (GelMA), already widely employed in regenerative medicine. Through a template-assisted polymerisation process, these polymers are structurally organised around biologically relevant target molecules, followed by template removal, yielding nanotraps with high-affinity, high-selectivity binding sites. This results in proteinaceous super-assemblies or nanogels, characterised by tunable supramolecular aggregation, eventually enriched secondary structures (e.g. ß-sheets), providing a biomimetic scaffold that can both interact with and modulate its biochemical environment. This strategy has been successfully applied to generate nanotraps capable of selectively binding key molecular targets such as albumin, hepcidin, and interleukin-6 (IL-6) [1, 2], demonstrating the versatility of the imprinting approach across a range of biologically relevant molecules. BioMIPs synthesised from biocompatible, polymerizable matrices exhibited nanomolar affinity, high selectivity, and remarkable stability, maintaining functionality for over 10 days in aqueous suspension and up to 6 months in lyophilised form. Their target-binding performance was validated in vitro, showing substantial depletion of target molecules from complex biological environments, while ensuring full cell viability. In addition, fluorescent labelling enabled effective imaging and internalisation studies in cell culture, supporting their potential use in diagnostic and therapeutic applications. Overall, these degradable and biocompatible supramolecular assemblies stand as a unique class of metamaterials that can find application for tissue regeneration. Their intrinsic recognition capability makes them ideal candidates for precision biointerfaces, selective modulation of disease pathways, and integration in tissue engineering scaffolds.

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Polymeric Nanomedicines for Targeted Cancer Immunotherapy

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Immunotherapy has transformed cancer treatment, but its efficacy is often hampered by the immunosuppressive tumor microenvironment (TME), which limits immune cell activity and promotes resistance. To address this, we have developed nanomedicine strategies that enable targeted immune activation while minimizing systemic toxicity. Thus, we engineered pH-sensitive polymeric micelles that accumulate in tumors via the enhanced permeability to delivering drugs to alter the TME for promoting antitumor immunity. Upon sensing this acidic environment, the micelles undergo conformational changes that trigger the release or activation of immune modulators. Using this platform, we delivered interleukin-12 (IL-12), a potent but systemically toxic cytokine, achieving localized immune activation and eradication of otherwise treatment-resistant tumors, such as triple negative breast cancer and melanoma, without inducing systemic adverse effects. To further amplify immune responses, we also designed nanosuperagonist micelles that co-deliver IL-15 and its receptor IL-15Rα, mimicking physiological trans-presentation and enhancing activation of $CD8^+$ T cells and natural killer cells. This co-delivery strategy within a single nanocarrier ensures synchronized signaling and robust immune stimulation, critical for overcoming the suppressive TME. Expanding on this platform, we integrated mRNA delivery to enable in situ cytokine production directly within the tumor milieu. Rather than relying solely on protein loading, we encapsulated mRNA encoding immunostimulatory cytokines, allowing the host cells to transiently produce therapeutic proteins. This strategy not only enhances control over cytokine dosage and kinetics, but also simplifies production by bypassing recombinant protein synthesis. To further restrict cytokine activity to the tumor, we developed light-activatable micelles that enable spatial and temporal regulation of mRNA translation. Using this approach, we achieved on-demand induction of IL-2 expression in tumors, reducing systemic exposure and controlling the pleiotropic effects of this cytokine. Our programmable micelle systems represent a powerful toolkit for overcoming immunosuppression and resistance in cancer therapy. By combining targeted delivery, controlled activation, and customizable cytokine formats, including both proteins and mRNA, we have established a flexible nanomedicine framework for next-generation immunotherapies with enhanced safety and efficacy profiles.

KEYNOTE LECTURES – Session 4
ALLAN HOFFMAN SESSION

Silk-ink for human health: A versatile platform for precision biomaterials

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Bioprinting is nowadays gaining an increased interest in the biomedical field, due to its capability to manufacturing matrices with controlled geometry, gradient, chemistry and functionality. In this context, precision biomaterials inks are under elaboration to recapitulate cells tissue-specific and fabrication requirements, balancing bioactivity and printability. Biopolymers market is having an increased interest, and sustainable and circular economy materials are more appealing source materials in terms of environmental impact and their multifunctionality and versatility. Nature-derived polymers are a new generation of materials with great potential in precision medicine and tissue engineering. Our group is strongly focused on the development of new precision biomaterial inks, with a wide range of peculiar properties, designing a technological platform based on the use of silk proteins in combination with other natural resources such as alginate and bioceramics. The talk will be focused on the development of strategies and products for 3D-bioprinted instructive matrices hydrogel-based, considering sustainable processing approaches, bioink design from crosslinking to printability and functionality, reproducibility and scale-up of the process. Aspects as process design, protocols standardization, reproducibility will be reported, also underlining warnings and critical aspects to be still optimized. Finally, it will be discussed some examples related to products for cornea, bone and myocardium regeneration.

Biohybrid and Fully Synthetic Polymer Hydrogels for Cell-Instructive Matrices

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Glycosaminoglycans (GAGs) within extracellular matrices (ECM) play a crucial role in modulating the presentation of soluble, cell-instructive signals, thereby influencing cell behavior and fate. Incorporating GAGs with distinct sulfation patterns into engineered polymer networks offers a powerful and versatile strategy to mimic native ECM functions and direct cellular responses in a controlled manner. We have developed a rational design approach for ECM-inspired hydrogels based on multi-armed poly(ethylene glycol), diverse GAGs, and functional peptides, enabling systematic exploration of their combinatorial effects on cell signaling.

Advanced microfabrication techniques—including cryogelation, solvent-assisted micro-molding, microfluidic microgel fabrication, and multicomponent inkjet bioprinting—facilitate the creation of multiphasic and multifunctional GAG-based hydrogels with finely tuned spatiotemporal signaling properties. This materials platform supports the development of sophisticated 3D culture models that recapitulate stem cell niches and tumor microenvironments, providing valuable tools for fundamental biological studies.

Beyond in vitro modeling, these hydrogels serve as promising scaffolds for innovative therapeutic strategies targeting chronic wounds and neurodegenerative diseases, where precise control over biochemical cues and matrix architecture is essential. By bridging biomolecular complexity with advanced fabrication, our approach paves the way for next-generation biomaterials that harness the cell-instructive power of GAGs to guide tissue regeneration and disease modeling.

Smart Healthcare Materials and Devices for Theranostic Applications

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Diagnostic and therapeutic devices have been routinely used in the clinic placed at patients' bedsides. However, with the recent progress of nanobiotechnology, a variety of healthcare devices have been investigated for theranostic applications with greatly improved patients' compliance. Here, we developed smart contact lenses and smart wearable devices for both continuous diabetic monitoring and diabetic retinopathy therapy. Smart contact lens could measure tear glucose levels as a non-invasive alternative to the conventional blood glucose tests and deliver drugs from gold coated reservoirs for the treatment of diabetic retinopathy. We also developed a smart NIR light emitting contact lens for the diabetic diagnosis and the treatment of diabetic retinopathy. The retinal vascular hyper-permeability induced by diabetic retinopathy in rabbits was reduced to the statistically significant level by simply wearing the NIR light emitting contact lens. In addition, we developed a smart contact lens to monitor and control the intraocular pressure (IOP) for the treatment of glaucoma. The IOP could be maintained in a controlled manner by the released drug in response to the measured IOP. On the basis of these results, we developed a smart wearable device for highly sensitive glucose monitoring in sweat for clinically feasible diabetic diagnosis. A blue-tooth system could send data wirelessly allowing patients to check their diabetic diagnosis results on the mobile phones. Furthermore, we developed cell-integrated poly(ethylene glycol) hydrogels for in vivo optogenetic sensing and therapy. The real-time optical readout of encapsulated heat-shock-protein-coupled fluorescent reporter cells made it possible to measure the nanotoxicity of cadmium-based quantum dots in vivo. Using optogenetic cells producing glucagon-like peptide-1, we performed light-controlled therapy and obtained improved glucose homeostasis in diabetic model mice. Taken together, we successfully developed smart wearable devices for optogenetic cellular engineering for diagnostic and therapeutic applications. This presentation will provide the current state-of-the-art smart healthcare materials and devices for further clinical applications.

KEYNOTE LECTURES - Session 5

Piezo4Spine: Novel strategies for neural repair after spinal cord injury

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Millions of people live and deal with the devastating consequences of spinal cord injury (SCI) worldwide. Despite outstanding advances in the field to both understand and tackle these pathologies, a cure for SCI patients, with their peculiar characteristics, is still a mirage [1]. Piezo4Spine is a multidisciplinary European project devoted to the development of effective therapeutics for neural repair after SCI [2]. By building a 3D therapeutic mesh, named as theramesh, we intend to deliver multiple pro-regenerative signals to the injured spinal tissue to overcome inhibitory processes and activate tissue repair. Some of the building blocks for this theramesh include iron oxide nanoparticles [3], natural hydrogels [3] and reduced graphene oxide scaffolds [4]. Motor training routines are included to synergistically potentiate the benefits of the theramesh [5]. These materials are all explored in vitro with primary cultures of neural cells from rat embryonic cerebral cortices and in vivo in cervical hemisected and thoracic transected rats. This talk will provide a journey through some of the most relevant findings of this research.

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Polypeptide-Based Nanomedicines: Enhancing Tropism and Overcoming Biological Barriers

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Polypeptides play a pivotal role in various domains, particularly in nanomedicine[1]. The physicochemical properties and biological performance of polypeptide-conjugates are dictated by a complex interplay of structural factors, highlighting the critical need for detailed structure–activity relationship (SAR) studies to inform the design of hierarchical polypeptide systems. Notably, this structural complexity is advantageous, as even subtle molecular alterations can yield significant and unexpected biological effects[1].

In our research group, we have addressed conventional challenges in polypeptide synthesis through precise, controlled reactions, enabling the creation of well-defined architectures via N-carboxyanhydride (NCA) polymerization[2]. Post-polymerization modifications further extend functionality, introducing a diverse array of orthogonally reactive attachment points[1 3]. Utilizing this modular, bottom-up approach, we have engineered polypeptides with varied architectures—including diblock copolymers and star-shaped constructs—that self-assemble into supramolecular nanostructures. The scale up of such assemblies have been optimised by mean of microfluidics, to yield nanocarriers that have demonstrate promising traits, such as, tissue specificity[4], subcellular compartment targeting[5], and potential for brain delivery[6].

Coupling this structural strategy with rational crosslinking approaches and polymer–drug linker design[4–7] has enabled extensive in vitro and in vivo evaluation. These systems show minimal toxicity, enhanced cellular uptake, prolonged systemic circulation, and targeted accumulation in specific sites such as lymph nodes[4], mitochondria[5], and the brain[6]. These effects are modulated by structural parameters including stiffness, deformability, charge, size, or shape.

Collectively, these findings position our polypeptide-based nanosystems as promising candidates for use as nanocarriers in therapeutic and diagnostic applications[8].

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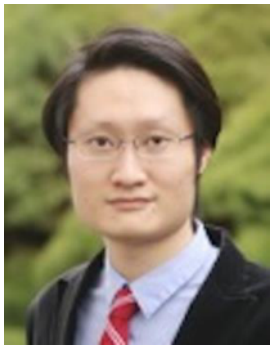

Unconventional additive (bio)manufacturing methods for Regenerative Medicine

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Over the last decades, the field of three-dimensional (3D) printing, or additive manufacturing, has witnessed tremendous progress. 3D printing enables precise control over the composition, spatial distribution, and architecture of the printed constructs facilitating the recapitulation of the delicate shapes and structures of target patterns. More recently it has been further combined with cells and cell-laden biomaterials to offer the versatility to fabricate biomimetic volumetric tissues that are both structurally and functionally relevant. Nevertheless, conventional 3D printing and bioprinting techniques are limited in certain aspects. This talk will thus discuss our recent efforts in developing a series of advanced additive (bio)manufacturing strategies that take unconventional approaches to tackle some of these problems and improve their capacities towards diverse applications in biomedicine with a focus on regenerative medicine. These platform technologies will likely provide new opportunities in areas from constructing functional tissues and microtissue models for promoting personalizable medicine, all the way to minimally invasive surgical implications.

KEYNOTE LECTURES - Session 6

Advances in biomaterials as artificial extracellular matrices in in vitro tumour models

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Biomaterials play a pivotal role in the modulation of cellular functions, extracellular matrix production, and in tissue regeneration and remodelling. The increasingly need for physiologically-relevant three-dimensional (3D) in vitro models as alternative to two-dimensional (2D) cell culture methods and animal models may pose different challenges in respect to the demand of novel and sustainable biomaterials with superior biomimetic functionalities. In this invited lecture, a concise overview on the relevant research dealing with the development of sustainable biomaterials to be used as artificial extracellular matrices (aECM) in 3D in vitro tumour models, including colorectal and breast tumour models, and glioblastoma, will be discussed. Other tissue engineered models that have been explored will be also presented (e.g. cartilage, bone, liver, brain-blood barrier). In brief, the latest 3B's research achievements in this topic together with the current advances in biofabrication strategies will be summarized, thus serving as a core reference for the training of a new generation of "Hybrid" students and established tissue engineering and regenerative medicine (TERM) researchers.

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Advanced 3D Bioengineered Tumor Models to Evaluate Targeted (Nano)Therapeutics

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The physical and biochemical characteristics of the solid tumors control their growth, invasion, and metastasis. The dense stroma also acts a physical barrier which in turn prevents penetration of (nano)therapeutics. Therefore, many therapeutics fail in preclinical animal models or during clinical development. The 2D cultures are too simple, and the in vivo models are too complex to understand the complexity of the tumor-stroma interactions. It is therefore imperative to develop advanced in vitro models that mimic the tumor stroma. In the past years, we have developed different 3D models to mimic various features of the stroma concerning different cancer types such as breast cancer, glioblastoma, pancreatic cancer using 3D multicellular spheroids, blood vasculature compression model, scaffold based microtumor and 3D bioprinted models (1, 2). In pancreatic tumor spheroids, gemcitabine reduced the spheroids growth but inhibition of stroma with our ITGA5 antagonist AV3 enhanced the effect of gemcitabine (3). These combined effects were confirmed in different mouse tumor models for pancreatic tumor. Furthermore, we mimicked the stroma-induced compression of blood vasculature in pancreatic tumor by creating blood vasculature in collagen/fibrinogen scaffold and studied the compression over several days (4). In addition to interactions with fibroblasts, we have also studied interactions of tumor cells with macrophages using 3D bioprinted glioblastoma model. In this model, we printed the mini brain with macrophages and introduced tumor cells and studied their interactions for migration, gene changes in view of clinical transcriptomics data (5). Altogether, these studies show the importance of 3D models in tumor stroma interaction which affect the therapeutic efficacy of chemotherapy. Therefore, these models will serve as excellent testing platforms for novel therapeutics before testing in animal models.

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The Polymer heaven for biomedical applications

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The seamless integration of electronics with living systems holds transformative potential Properties of polymers used in biomedical applications and mostly as biomaterials differ depending on the need. The required application could be a temporary implant where one can use a biodegradable or biostable polymer. The material could be designed for use with cells where it may be needed as a cell carrier within or on the polymeric implant. In the previous case one can use a soft hydrogel type of material which needs a high temperature at some stage of the processing or in the case of cells attached on the implant is acceptable then it could be a selection from a large group of thermoplastic polymers. These polymers could be used as biomaterials or as carriers for tissues or cells. In one application where a load bearing and biodegradable polymer was needed a thermoplastic polyester, poly(ε-caprolactone) (PCL) was used along with hydroxyapatite to provide extra strength. In another study a surface needed for a study involving tissue healing property a nondegradable, soft polymer needed was polydimethyl siloxane (PDMS, silicone) was used. In case of a 3D printing material was needed with biodegradability the material used was hyaluronic acid. In this presentation examples of polymer applications with very different requirements and for use under very different conditions will be presented these will include modified, degradable, transparent and highly hydrophilic biological hydrogels of gelatin for corneal stroma produced by 3D printing, stiff, synthetic, biodegradable segmental bone implants of PCL, and nondegradable, soft, synthetic polymers as tissue regeneration platforms of PDMS.

Taking mRNA Therapeutic Potentials to the Next Level: Enhancing Bone Regeneration through Rational RNA Combinations

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Messenger RNA (mRNA)-based therapeutics have emerged as a transformative strategy in regenerative medicine, offering precise and transient expression of key regenerative factors. Our previous work has demonstrated the strong osteoinductive potential of a chemically modified BMP-2 mRNA for bone regeneration. In this keynote, we will highlight the unique regenerative profile of a sister molecule, BMP-7 mRNA, which induces specific gene and protein expression patterns that underscore its distinct superiority in certain contexts of bone healing. Furthermore, we extend these findings by exploring the added value of rational mRNA combinations in mimicking the complex signaling milieu of native tissue repair. We present new data showing that the co-delivery of BMP-2 and BMP-7 mRNAs results in significantly enhanced osteogenic outcomes compared to single-factor strategies. In addition to osteogenesis, we demonstrate that critical regenerative processes such as angiogenesis and innervation can be effectively stimulated through combinatorial mRNA approaches. This work underscores the potential of multi-target mRNA formulations in designing next-generation therapeutics for musculoskeletal regeneration.

KEYNOTE LECTURES - Session 7
ASIAN-PACIFIC SESSION

Biomaterial-based tissue regeneration therapy based on natural self-healing potential and inflammation

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For tissue regeneration therapy based on the natural self-healing potential of patients, it is practically important to manipulate the inherent ability of cells for their proliferation and differentiation which physiologically contributes to the natural self-healing potential. However, only when cells with high potentials are transplanted without considering any their local environment, the cell-based tissue regeneration cannot be always expected to be realized. As the body environment, inflammation often affects the therapeutic efficacy of cells. Inflammation is one of the essential host responses to pathologically modify the process of tissue regeneration and repairing. Without inflammation, no tissue regeneration takes place.

We have developed biomaterial technologies which give cells a local environment to enhance their ability for tissue regeneration and repairing. A key bio-signaling molecule was supplied to the right place at the right time and concentration by utilizing drug delivery system (DDS) technology, Consequently, the body system initiates to physiologically function, resulting in the natural induction of cell-based tissue regeneration. A cell scaffold of biomaterials provides cells of their good local environment to show their functions of tissue regeneration. A suitable combination of DDS and cell scaffold technologies enabled cells to achieve tissue regeneration. After inflammation was modified by the DDS system of anti-inflammatory drug, the subsequent biomaterial-based activation of cell function augmented the therapeutic efficacy of cell-based tissue regeneration. Among inflammation cells, macrophages were focused. Macrophages are physiologically classified into two types of pro-inflammatory (M1) and anti-inflammatory polarization (M2). In case M2-type macrophages interact with stem cells, the inherent ability of stem cells was promoted to achieve cell-based tissue regeneration.

Enhancing Antibacterial Efficacy: Leveraging Stimuli-Responsive Mechanisms to Modulate Reactive Oxygen Species in Nanoparticle Design

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Post-implantation infections in orthopaedics, particularly those linked to biofilm formation, result in a significant threat to patient outcomes. Traditional antibiotic therapies are hampered by their limitations, particularly in effectively eradicating bacteria while modulating osteoimmunological responses. Once an infection manifests, it often requires a lengthy course of conventional antibiotics, which contributes to the emergence of drug-resistant bacteria. Alarmingly, over 40% of drug-resistant Staphylococcus aureus strains are methicillin-resistant (MRSA), underscoring a critical global healthcare challenge associated with orthopaedic implant infections. This persistent threat necessitates the urgent development of innovative antimicrobial strategies.

In this context, we showcase our novel antibacterial nanoparticles (NPs) designed to generate reactive oxygen species (ROS) in response to external stimuli, such as near-infrared (NIR) radiation, ultrasound, and microwave irradiation. These stimuli-responsive nanoparticles leverage their unique physicochemical properties to enhance antimicrobial efficacy while minimizing side effects. Our investigation will elucidate the mechanisms of ROS generation through various stimulation modalities, highlighting the importance of nanoparticle composition and surface functionalization for optimizing both efficiency and specificity. We also demonstrate the synergistic effects realized through the combination of antibacterial nanoparticles and conventional antibiotics, ultimately improving antibacterial performance. These thoughts are tailored to accommodate diverse micro-environmental conditions and specific clinical scenarios. Furthermore, we will discuss the implications of this innovative technology in combating biofilm formation and persistent infections while maintaining high levels of biocompatibility and safety. By elucidating the intricate interactions between stimuli and nanomaterials, our findings are set to inspire future research and technological advancements in the field of antibacterial nanoparticles.

Rational Polypeptide Design via Database Integration: Applications in Scaffolds and Mitochondrial Gene Delivery

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Over the past few decades, biomaterials research has seen rapid progress, particularly in the exploration of targeted biomaterials design. Polypeptides have emerged as a promising avenue in this endeavor due to their ability for rapid manipulation and alteration based on their primary and secondary structures. Through various noncovalent interactions, peptides can self-assemble into biomaterials, offering vast potential across diverse fields like biotechnology. Applications range from tissue engineering to cargo delivery, biocatalysis, and energy storage. Furthermore, peptides chemical specificity allows for systematic refinement and manipulation of their higher-order structures, facilitating the discovery of novel sequences with tailored properties such as solubility and stability to different environmental factors. In the recent years, this has included computational design of novel sequences through AI-driven as well as machine learning to discover novel motifs with properties such as fibril formation or other higher order structures. We have recently established the use of peptide microarrays for high-throughput screening of peptide stability. Sequence analysis through motif identification and machine-learning based cluster analysis was performed to yield completely new peptides that were tested in enzymatic degradation assays. Furthermore, integration of these sequences into other biomaterials have shown to alter their physical properties and could be used to guide future biomaterial design. Another example is rational polypeptide design via database integration for mitochondrial gene delivery. In this study, we propose a simple yet effective mitochondrial gene delivery system comprising an artificial peptide inspired by a transmembrane mitochondrial membrane protein database. The designed mitochondria-targeting peptides presented on the carrier surface effectively guide the encapsulated plasmid to the mitochondria, facilitating mitochondrial uptake and gene expression. The developed system successfully delivers exogenous mtDNA to mtDNA-depleted cells and leads to simultaneous multigene expression, ultimately restoring mitochondrial functions, including the mitochondrial respiration rate. The established multiple gene expression system in each mitochondrion is a game-changing technology that can accelerate the development of mitochondrial engineering technologies as well as clinical applications for mitochondrial diseases.

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Nanozymes-armed microbes for disease treatment

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Probiotic therapy demonstrates outstanding therapeutic effects in various diseases by positively regulating the composition and function of the probiotic microbiota, actively modulating host immunity and metabolism. The application of gene editing technology has greatly enriched the functions of probiotics and enhanced their efficacy. Recently, the rapid development of nanomaterials and technologies has opened a new pathway for improving probiotics' efficacy. The probiotic/nanomaterial hybrids formed by probiotics and functional nanomaterials can possess both the biological activity of probiotics and the special physicochemical properties of nanomaterials, achieving complementary advantages or synergistic effects to enhance the efficacy and translational potential of probiotics in a more convenient way. The efficacy of probiotics mainly relies on the action of the biological enzyme system. Nanozymes are a type of nanomaterials with catalytic functions similar to natural enzymes and are more stable than natural enzymes. Among them, redox nanozymes can mimic the activities of peroxidase (POD), catalase (CAT), superoxide dismutase (SOD), and others, modulating energy metabolism and signaling related to redox reactions. Aiming to regulate probiotic function, we prepared probiotic/nanozyme hybrids based on the metabolic regulatory properties of redox nanozymes to supplement the enzyme system lacking in probiotics or to enhance their existing enzyme system. We used Fe-based single-atom nanozymes with CAT and SOD activities to supplement the antioxidant enzyme system lacking in anaerobic Bifidobacterium longum. Nanozymes can sustainably, robustly, and efficiently help probiotics resist the attack of high concentrations of reactive oxygen species (ROS) in inflammatory intestines, prolonging their colonization time in the inflammatory intestines and enabling them to exert a more efficient role in microbiota regulation. This probiotic-antioxidant nanozyme hybrid material has shown good therapeutic effects in mouse and dog models of inflammatory bowel disease (IBD) and is expected to become a new formulation to replace traditional IBD drugs.

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KEYNOTE LECTURES - Session 8
ASIAN-PACIFIC SESSION

Biomaterials for immunoisolation and tissue adhesion, and anti-adhesive barriers

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Pancreatic ß cell therapy for type 1 diabetes faces major hurdles, including low cell survival due to physical stress and aggressive immune responses. This seminar introduces a novel multilayer hydrogel nanofilm caging strategy designed to enhance ß cell protection and prolong their functionality. The hydrogel nanofilm, composed of monophenol-modified glycol chitosan and hyaluronic acid, is formed via tyrosinase-mediated enzymatic cross-linking, creating a nano-thin protective layer around the cells. This innovative approach not only shields cells from high shear stress but also mitigates immune responses by disrupting cell-cell interactions. Using a xeno-islet cell transplantation model, we demonstrated that hydrogel nanofilm-coated ß cells successfully transplanted via the intraportal route regulated blood glucose levels in a type 1 diabetes animal model for over 250 days without requiring immunosuppression. This strategy shows transformative potential as a platform for cell-based therapies, significantly improving cell viability and therapeutic efficacy. In addition to exploring tyrosinase-mediated cross-linking for immunoisolation, this talk will also discuss broader applications, including the development of paintable hydrogels for wet adhesive environments and charge-dependent biomaterial-immune cell interactions to reduce immune cell infiltration. Together, these findings highlight the versatility and promise of biomaterials engineering technologies in advancing therapeutic innovation.

Elastin-based hydrogels promote wound healing by regulating the tissue immune microenvironment

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The tissue immune microenvironment plays an important role in wound healing. It is of great significance to develop bioactive repair systems that can regulate immune cells within tissue microenvironment to promote wound repair. Our team found that blue light cross-linked elastin hydrogels derived from mammalian extracellular matrix elastin can recruit a large number of neutrophils and M2 macrophages during acute skin wound repair process in mice model, thereby promoting angiogenesis and collagen deposition in the wound site. Furthermore, single-cell RNA sequencing (scRNA-seq) analysis of mice skin wound tissues revealed that the proportion of Ccl3+ Neutrophils and M2 Macrophages in the elastin group (ELN) was significantly higher than that in the gelatin control group on days 5 and 7 post-surgery. In vitro, the conditioned medium of elastin-based hydrogels co-cultured with neutrophils can promote macrophages toward M2 polarization. In addition, the scRNA-seq analysis results of macrophage subset proportions were combined with pseudo-time series analysis, and it was found that the ELN may promote macrophages to express Fau on the 3rd day post-surgery, increase the proportion of Ccl7+ Macrophages, and participate in regulating the inflammatory response of the wound. On the 5th and 7th days of wound treatment, the ELN may promote macrophages to express IL10, increase the proportion of M2 Macrophages, and promote wound repair. Cell interaction analysis showed that elastin-based hydrogels may regulate macrophages through the TGF-ß pathway, thereby promoting the proliferation of fibroblasts and the production of collagen fibers.

Smart Polymer Technologies for Global Health

Mitsuhiro Ebara

Research Center for Macromolecules and Biomaterials, National Institute for Materials Science (NIMS)

We have been developing smart polymers (stimuli-responsive polymers) for biomedical applications in the last 20 years. Especially our temperature-responsive polymer-antibody conjugates have been applied for more than 1000 patients with hepatitis C virus to improve the sensitivity of rapid test. I will talk about our screening campaign in African countries.

Development of Functional Scaffold Biomaterials and Bioactive Molecules from Natural Resources

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Regeneration of bone and cartilage tissues remains a challenging clinical problem. Conventional scaffolds suffer from significant limitations including donor scarcity, immunogenicity, and suboptimal biocompatibility. These constraints necessitate the development of sustainable, high-performance biomaterials capable of actively promoting bone and cartilage tissue regeneration. This study aimed to engineer scaffolds with tunable properties and enhanced bioactivity from underutilized natural resources, specifically animal-derived by-products. We hypothesized that these sustainable natural sources could be transformed into advanced biomaterial platforms for superior tissue regeneration applications.

Our approach involved extraction of biomaterials from novel natural sources including duck feet-derived collagen and Ogolgye chicken-derived demineralized bone particles (DBP). These materials were fabricated into diverse platforms including porous scaffolds, injectable hydrogels, and shape-memory polymers. Bioactive molecules such as polydeoxynucleotide (PDRN), TGF-β3, and BMP2 were incorporated to guide osteochondral tissue regeneration responses. Efficacy was evaluated through comprehensive in vitro cell studies using bone marrow mesenchymal stem cells and chondrocytes, along with in vivo animal defect models. Duck feet collagen scaffolds demonstrated accelerated bone mineralization while reducing inflammatory responses. Ogolgye-derived DBP sponges containing natural melanin exhibited the highest expression of osteogenic markers (ALP, Col 1). For cartilage applications, PDRN-loaded hydrogels upregulated chondrogenic genes (COL2, SOX9), while TGF-β3 delivery systems effectively regenerated cartilage defects. Additionally, tannic acid-crosslinked gelatin scaffolds displayed rapid shape-memory behavior with superior recovery rate, making them ideal for minimally invasive surgical procedures. This work demonstrates comprehensive approaches for creating advanced biomaterials derived from eco-friendly natural sources. Through exploiting the inherent biological properties of these neglected resources, we offer viable and clinically applicable solutions to improve therapeutic outcomes for bone and cartilage defects.

KEYNOTE LECTURES - Session 9

Beyond barrier crossing: Nanomedicine as a therapeutic strategy for blood-brain barrier repair in dementia

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Nanomedicine emerged from the necessity to bypass biological barriers and achieve targeted drug delivery—maximizing therapeutic efficacy while minimizing systemic toxicity. A paramount challenge in this field has been the blood-brain barrier (BBB), a highly selective interface that restricts access to the central nervous system (CNS), rendering most neurological disorders, including Alzheimer's disease (AD) and other dementias, notoriously difficult to treat. Traditional pharmacology has struggled to overcome this obstacle, but advances in supramolecular chemistry have enabled the rational design of nanoscale carriers capable of crossing or bypassing the BBB. These systems, typically ranging from tens to hundreds of nanometers, leverage tailored surface chemistries and dynamic interactions to facilitate CNS delivery. Yet, what began as a drug delivery challenge has evolved into a deeper biological insight: the BBB is not merely an obstacle but a therapeutic target in itself. Emerging evidence suggests that BBB dysfunction is not just a consequence but also a contributor to neurodegeneration. Vascular deficits, impaired clearance mechanisms, and chronic neuroinflammation all play critical roles in diseases like AD. Consequently, strategies designed to traverse the BBB have revealed an unexpected opportunity—repairing the barrier itself. By restoring proper BBB function, we can correct metabolic imbalances, enhance toxin clearance, and mitigate neuroinflammatory cascades, thereby addressing core pathological mechanisms of dementia. In this talk, I will discuss how nanomedicine has shifted from passive drug transport to active vascular engagement. Supramolecular therapeutics can now be engineered not only to deliver payloads but also to remodel the cerebrovascular interface, promoting BBB integrity and function. I will present evidence that such approaches can reverse key aspects of neurodegeneration, offering a novel therapeutic axis beyond conventional receptor modulation. Furthermore, the multivalent nature of nanoscale scaffolds allows for unprecedented control over receptor clustering, endocytic trafficking, and signaling—enabling interventions that go beyond simple inhibition or agonism. Ultimately, the lessons learned from BBB-targeted nanomedicine extend far beyond delivery. They redefine how we approach neurological therapy: not just by treating symptoms but by restoring the brain's physiological microenvironment. This paradigm opens new avenues for tackling AD and other neurodegenerative disorders, where vascular repair and barrier normalization may prove as critical as direct neuronal rescue.

Bioelectricity in Tissue Engineering: The role of electrical stimulation and electroconductive biomaterials in macrophage function and spinal cord therapeutics

Michael Monaghan

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Modulating the immune response has emerged as a promising strategy to combat degenerative disease and promote effective tissue repair. While numerous immunomodulatory strategies currently exist, their limitations including suboptimal efficacy and specificity, highlight the ongoing need to explore alternative approaches. Electricity pervades throughout all the body at an organ, tissue and cellular scale with frontier biomaterial and tissue engineering approaches seeking to harness this towards regeneration and repair.

Studies to date, regarding the effects of electrical stimulation on macrophages are limited, specifically in the context of primary human cells. Electrical stimulation exhibits an immunomodulatory effect on primary human macrophages, promoting an anti-inflammatory pro-regenerative phenotype, accompanied by M2 macrophage polarisation, decreased inflammatory macrophage marker expression, as well as enhanced expression of angiogenic genes and driving wound healing in a scratch assay. This endorses electrical stimulation as a novel therapeutic strategy for the modulation of macrophages, across multiple injury and defence microenvironments.

These observations also translate to spinal cord injury (SCI) which remains a major clinical challenge due to its complex pathophysiology and lack of effective treatments. While electrical stimulation (ES) offers therapeutic potential for promoting neural repair, its clinical translation is limited by the invasiveness of conventional systems. Here, we report a non-invasive wireless electrical stimulation (WES) platform based on charge polarisation-induced capacitive coupling, enabled by a conductive silk fibroin/PEDOT:PSS (SF/PEDOT) hydrogel. SF/PEDOT hydrogels exhibit a tuneable mechanical stiffness (2-60 kPa), injectable delivery with (<5 N peak force), and electrical conductivity (~0.3 S/m) closely matching the spinal cord. This hydrogel platform supports efficient non-invasive capacitive coupling for secondary field transduction at low frequencies (10 kHz). Using this WES system (2 V, 10 kHz), we drive human blood-derived macrophages (hBDMs) toward a reparative phenotype, while downregulating proinflammatory markers even under inflammatory conditions. In parallel, hiPSC derived cortical astrocytes (CTX-ASTRO) encapsulated within SF/PEDOT hydrogels showed enhanced functional maturation under WES, evidenced by upregulated Cx43 gap junction protein expression. In an in vitro SCI-like model of reactive astrogliosis, WES via SF/PEDOT partially mitigated astrocytic reactivity by reducing IL-6 and CXCL10 secretion and increasing Cx43 expression. Conditioned media from WES treated CTX-ASTRO further suppressed proinflammatory activation of hBDMs. Together, these results provide the first evidence of the dual neuroprotective and immunomodulatory potential of a non-invasive, conductive hydrogel-based WES platform, validated using two human cell types specific to SCI pathophysiology. Thus, this approach offers a minimally invasive, translational solution for spinal cord repair via neuromodulation.

Design of magneto-responsive, fiber-hydrogel composites to enable three-dimensional spatial and temporal control over fiber alignment

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KEYNOTE LECTURES - Session 10

Generation and clinical translation of a Fibrin-Agarose bioengineered human cornea generated by tissue engineering

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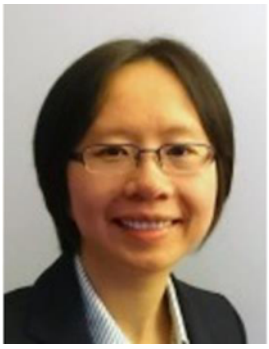
The clinical management of severe conditions affecting the structure of the human cornea is very complex, due to the limited regenerative capacity of this organ. In response to this challenge, we have recently developed a bioengineered human cornea substitute by tissue engineering named NANOULCOR. This corneal model consists of a stromal substitute composed of human corneal keratocytes immersed within nanostructured fibrin-agarose biomaterials with a stratified corneal epithelium on top, resembling an anterior human lamellar cornea. NANOULCOR was grafted in laboratory animals and demonstrated high biocompatibility and regenerative potential on the rabbit eye, with no detectable side effects. In addition, a thorough histological, histochemical and immunohistochemical characterization of the epithelial layer of these corneal substitutes demonstrated the expression of the corneal markers pancytokeratin, crystallins αa and λ and the cell-cell junction proteins CX43 and TJP1, along with the limbal markers KRT3, KRT19, KRT15, and ΔNp63. These preclinical results allowed us to evaluate the safety level of NANOULCOR in patients with severe corneal ulcers refractory to treatment in a preliminary phase-I advanced therapies clinical trial with good results. In these moments, a phase-II clinical trial has been implemented to determine functionality of this ATMP as compared to the gold-standard treatment consisting in the implant of an amniotic membrane. These results confirm the potential usefulness of NANOULCOR anterior lamellar corneal substitutes in patients with severe corneal ulcers.



Electronic Spider Silk-Mimetics for Skin-Imperceptible Bioelectronics

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The seamless integration of electronics with living systems holds transformative potential for health monitoring and environmental sensing. However, such bioelectronic interfaces must preserve the native sensory and physiological functions of their hosts while minimizing environmental impact. Here, we report a strategy for the imperceptible augmentation of biological surfaces through the in situ tethering of mixed conducting microfibres. These solution-drawn fibres, reminiscent of electronic spider silk, are directly deposited onto living substrates in a semi-wet state, enabling conformal, single-step integration. The fibre architecture is tunable, allowing adaptation to diverse morphologies and surface textures. We demonstrate this approach across a range of biological targets—including human fingertips, chick embryos, and plant leaves—where the resulting air-permeable, ultrathin layers maintain native appearance and function while imparting electronic and sensing capabilities. Furthermore, the fibres can interface with prefabricated microelectronics and textiles, and are amenable to repair, upgrade, and recycling. This work establishes a versatile platform that bridges advanced materials, biofabrication, and tissue engineering, opening new avenues for personalized healthcare, soft robotics, and biohybrid systems.

Nature-derived, photo-actuated biomaterials for the fabrication of functional biodevices

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A transitional phase in the evolution of bioelectronics is witnessing a shift from rigid components to soft and flexible systems. Such next-generation devices have a broad range of biomedical applications, including electronic skins, soft robotics, tissue engineering, and wearable or implantable biosensors for continuous monitoring. Bioinspired and bioderived materials provide an exciting pathway towards creating precision medicine and advanced personalized tools, while addressing issues of material sustainability and mitigation of electronic waste. In this talk we will discuss different nature derived materials including silk proteins and gelatin for the fabrication of functional devices. Such biomaterials can serve as both the passive and active components either by themselves or as composites with a diverse set of multifunctional materials. We will discuss work from our group in transitioning to natural precursors and biocomposites for use as wearable sensors and implantable devices, biophotonic elements, energy-storage devices, assistive technologies, and human-machine interfaces.

Of specific interest are the proteins fibroin and sericin from the silkworm cocoon. Both biomaterials have a unique palette of properties that make them extremely versatile and viable candidates for soft (bio)electronics in diverse forms. A key modification in the proteins to render them photocrosslinkable allows integration with microfabrication processes. High resolution, high-fidelity bio devices can be formed in both rigid and flexible formats in two and three dimensions. Composites with organics such as conducting polymers provide added functionality, together with tunable properties, biocompatibility, and biodegradability, which provides prospects for sustainable engineering of devices. Such devices can be interfaced with soft tissue to provide two-way communication. Similarly, we discuss tunable composites such as photocrosslinkable fibroin-gelatin composites comprising photofibroin with photogelatin. The resulting composite (photofibrogel) has tunable properties for precise macroscale and microscale patterning, is biocompatible and can be modified with electrically conductive micropatterns for cell guidance and stimulation. Elastomeric composites with polydimethylsiloxane that are optically transparent and shelf-stable over 6 months are also discussed.
The ease of fabrication, biochemical functionalization, biocompatibility, as well as tunable mechanical properties and biodegradation of these biomaterials provide unique possibilities as sustainable, bioresorbable devices for regenerative medicine and personalized healthcare applications.

Multifunctional platforms for cell sensing in heterogeneous systems

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The microenvironment of degenerative pathologies and post-traumatic injuries is highly heterogeneous and dynamic, characterized by the establishment of pH and oxygen gradients due to altered cellular metabolic activity and impaired tissue perfusion. [1] This significant heterogeneity greatly influences the efficacy of therapeutic strategies aimed at tissue repair and regeneration.[2] To unravel these complex interactions, dynamic and high-resolution mapping of key microenvironmental parameters, such as pH and oxygen levels, is essential. Such mapping provides fundamental insights into how local gradients influence cellular morphology, function, and recovery potential. Various imaging and sensing techniques have been developed and applied in research and clinical settings to visualize and monitor cellular responses in these microenvironments.[3] Among these, ratiometric fluorescence-based sensors have proven to be powerful tools for non-invasive tracking of dynamic changes. This talk discusses the synthesis and application of nanostructured materials with an emphasis on their potential in microenvironment sensing. Examples include the use of extracellular matrix-mimicking electrospun nanofibers [4-7] and hydrogels [8-9] engineered for non-invasive spatiotemporal mapping of pH and oxygen changes in 3D in vitro models, underscoring the possibility of using these systems for personalized therapeutic development in the context of tissue degeneration and trauma recovery.

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Polymeric dry powder formulations of antibiotics and quorum sensing inhibitors for the treatment of lung infections

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Drug delivery systems (DDS) in the form of dry powder for inhalation play an important role in the management and treatment of pulmonary diseases. They are engineered to provide accurate tissue targeting and controlled release of active pharmaceutical ingredients (APIs) to the defined place in the respiratory tract to minimise systemic exposure. Such objects in which APIs are encapsulated within a biocompatible protective shell are designed to penetrate mucus and ensure controlled API release at the action site [1]. Polyanhydrides, which degrade through surface erosion, are excellent candidates to produce such advanced DDS to the lungs. In our group, we are working on polyanhydride DDS of antibiotics and quorum sensing inhibitors (QSi) for the treatment of bacterial infections in patients with chronic obstructive pulmonary disease (COPD) or cystic fibrosis (CF) exacerbations. Such DDSs have a form of microparticles made of poly(sebacic acid) derivatives loaded with antibiotics (gentamycin, tobramycin, and azithromycin) and QSi (curcumin, linolenic acid). We found that different antibiotics, particularly gentamycin, when administered in combination with linoleic acid, can be equally effective in combating drug-resistant bacteria in the biofilm form as when administered at doses 32 times higher [2]. We designed the microparticles to be (1) a suitable size for inhalation (aerodynamic diameter in the range of 1-5 μm, very good flowability), (2) have a neutral surface potential that helps penetrate mucus, (3) degrade quickly in 3 days and release the drug cargo, which is (4) capable of killing pathogenic bacteria in the planktonic form and preventing biofilm formation [3]. The system is cytocompatible with lung epithelial cells, as shown by in vitro tests, and histocompatible with lung tissue, as shown by ex vivo tests in a rodent model [4]. Acknowledgements: This study was supported by the National Science Centre Poland (2019/35/B/ST5/01103).

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KEYNOTE LECTURES - Session 11

Do cells like better rock music or classic music? A sonomechanobiology journey into orchestrating tissue regeneration

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A key challenge in tissue and organ regeneration is enhancing stem cell–material interactions to restore native functionality. Current strategies include the delivery and surface functionalization of biological factors, surface topography modifications, and the tuning of bulk and structural mechanical properties in 3D porous biomaterial constructs. While these approaches have successfully stimulated cell activity, their spatial and temporal control remains limited, restricting the regeneration of complex tissues. Here, we present examples where the integration of biofabrication technologies has enabled the design of a library of biological constructs with precisely tailored biological, physicochemical, and mechanical properties at multiple scales. These constructs facilitate cell-material interactions that modulate stem cell behavior, supporting tissue regeneration.

Beyond static design principles, we also explore the use of acoustic waves and magnetic fields as external mechanical stimuli to dynamically influence stem cell fate within 3D scaffolds. These externally triggered stimulation offers a non-invasive and finely tunable approach to activate mechanotransduction pathways, enhancing cellular responses in a controlled manner. Future efforts should focus on advancing these converging technologies to achieve precise, multi-scale control over stem cell activity, enabling the regeneration of complex tissues with vascular and neural networks. Such advancements will enhance in vivo integration and help bridge the gap from tissue to organ regeneration, ultimately bringing regenerative medicine technologies closer to clinical translation.

Functionalized substrates and nanostructures for advanced therapies

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Among the various possible embodiements of Advanced Therapies and in particular of Tissue Engineering, the use of temporary scaffolds to regenerate tissue defects is one of the key issues. The scaffolds should be specifically designed to create environments that promote tissue development and not merely to support the maintenance of communities of cells. To achieve that goal, highly functional scaffolds may combine specific morphologies and surface chemistry with the local release of bioactive agents. A desirable aspect to be considered in the design of those constructs is its sustainable fabrication.
Many biomaterials have been proposed to produce scaffolds aiming the regeneration of a wealth of human tissues. We have a particular interest in developing systems based in biodegradable polymers. Those demanding applications require a combination of mechanical properties, processability, cell-friendly surfaces and tunable biodegradability that need to be tailored for the specific application envisioned. Those biomaterials are usually processed by different routes into devices with a wide range of morphologies such as biodegradable fibers and meshes, films or particles and adaptable to different biomedical applications. For advanced therapies combining the scaffold with cells, it is critical to design scaffolds with adequate porosity enabling inner cell colonization and stimulating cells to attach and grow enabling obtaining a volume of neo-tissue. Furthermore, it is important to optimize the surface properties to provide the needed cues for the cells to differentiate into a stable phenotype conducive to the desired tissue regeneration and to ensure an adequate interaction with the host tissues.
This talk will review the basic concepts required for the development of natural-based biomaterials and scaffolds in combination with stem cells for advanced biomedical devices and therapies also considering its sustainable fabrication.

Smart Polymers: Towards future applications

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Introduction: Smart polymers respond to external stimuli by changing their physical and/or chemical structures and adapt themselves to their surroundings. The functional groups of the polymers have a broad spectrum, and their responsiveness can be against various stimuli such as temperature, pressure, magnetic field, light, sound, electric field, pH, ionic strength, specific molecules, etc. They can have dual or multi-responsiveness and can be used in complex sophisticated applications. These properties make them required materials for special applications from healthcare to aerospace. Applications: In the medical field, the smart polymers which swell or shrink depending on the temperature or pH are useful for targeted drug delivery systems to tumors; the ones which respond to electric fields and magnetic fields are used in sensors, actuators, and robotics are commonly used1. Stents that expand at body temperature; polymers that act like muscles with electrical signals; polymers that have self-repair property; tissue engineering scaffolds which support tissue regeneration depending on the stimuli of the surrounding tissue; hydrogels used as wound dressings can detect and adapt themselves to varying humidity and fluid content of the wound and provide the needed healing environment; wearable technology that can effectively interface with the human body to monitor various physiological changes and provides critical information necessary for the development of point-of-care diagnostics; even robot construction are all some examples for the applications of smart polymers. Addition of Artificial Intellenge (AI) in/on the smart polymers enhance their capability. A skin patch which provide various health metrics, including blood pressure and heart rate is an example. In the meantime, there are more advanced examples of wearable technology include AI, such as hearing aids, Meta Quest and Microsoft's HoloLens, a holographic computer in the form of a virtual reality (VR) headset, etc. Conclusion: Smart polymers are getting more and more attraction every day and increasing demand is existing in industry. In the meantime, intense chemistry is needed for the synthesis of multifunctional polymeric molecules; strong engineering is required to design the responsive systems; and deep understanding of biology is essential to study the effects in the biological systems.

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Engineering Vascularized Stroma for In Vitro Modeling of Human Tissues and Disease

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The ability to engineer vascularized stromal tissue is increasingly recognized as a critical step toward advancing both regenerative medicine and in vitro tissue modelling. Stromal compartments – including microvessels, fibroblasts, and extracellular matrix (ECM); play a fundamental role in recapitulating the structural and functional complexity of native tissues. Their integration into organoid-based and other 3D in vitro models is essential not only for promoting tissue maturation and physiological function, but also for creating more predictive platforms to study development, disease mechanisms, and therapeutic responses. This lecture will present an overview of strategies developed in our laboratory to engineer vascularized stroma in vitro. These include the design of ECM-mimetic hydrogels and the use of modular vascularized microtissues as building blocks to support the bottom-up formation of stroma-embedded microvascular networks. We will also highlight the development of perfusable organ-on-chip platforms that allow integration of vascularized stroma with epithelial organoids under dynamic flow conditions. These systems have been applied to improve the viability, structural organization, and functional maturation of organoid cultures, as well as to recreate fibrotic microenvironments relevant to pathological states. Together, these examples demonstrate how engineering vascularized stroma can enhance the biological complexity, physiological relevance, and translational potential of 3D in vitro models.

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KEYNOTE LECTURES - Session 12

Engineered biomaterials for regeneration and mechanobiology

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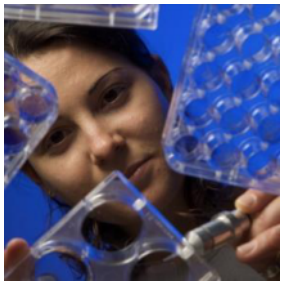
The physical properties of the extracellular matrix (ECM) and the use of growth factors are powerful tools to control cell behaviour, including fundamental processes such as cell migration and (stem) cell differentiation. Integrins are mechanotransductors that feel and respond towards the mechanical properties of the ECM. We have developed material systems that allow simultaneous stimulation of integrins and growth factors receptors. We have engineered polymers and 3D hydrogels that unfold and assemble proteins to allow exposure of the integrin and growth factor binding regions. For example, we show the use of BMP-2 in synergy with $\alpha 5\beta 1$ integrins to promote osteogenesis and regeneration of critical-sized defects. Further, we have developed interfaces that bind latent proteins that induce integrin-mediated mechanical activation of growth factors. We will demonstrate the use of TGF-$\beta 1$ that is released and activated by using engineered surfaces that organise fibronectin.
In the second part of the talk, we will use surfaces of controlled viscosity in our pathway to engineer and understand the viscoelastic properties of the ECM. We use supported lipid bilayers that are functionalised with either RGD (integrin binding) or HAVDI (cadherin binding) to demonstrate the molecular clutch is engaged on surfaces of high enough viscosity and, importantly, that it is weaken upon N-cadherin binding, controlled by the competition between vinculin and α-catenin for actin filaments. We then introduced substrates of controlled elasticity and viscosity, first in 2D using polyacrylamide hydrogels that were further patterned using fibronectin and then in 3D using PEG-hydrogels functionalised with fibronectin. We will discuss the unexpected interplay between viscoelasticity, cell adhesion and molecular clutch engagement.



Manufacturing of Natural-based nano-in-micro hydrogels for controlled site specific delivery of therapeutic agents

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Technological advances in drug formulation and delivery strategies have enabled site-specific drug delivery approaches, such as the localized treatment of tumors. To achieve controlled release at the target site, new generations of nanoparticles/nanovesicles are being engineered and embedded within natural-based nano-in-micro hydrogels.
By investigating the interaction between engineered nanoparticles or vesicles and hydrogel matrices, composite hydrogels were developed as promising candidates for minimally invasive drug delivery ensuring localised and sustained release of therapeutic agents at defined doses. These systems combine the controlled release capabilities of nanoparticles/vesicles with the biocompatibility and injectability of natural hydrogels.
Alginate- and pectin-based hydrogels were manufactured and loaded loaded with therapeutic nanoparticles/nanovesicles. The deployment of composite injectable alginate-based hydrogels in 3D printing was used as case study. Printability of natural-based biomaterial inks loaded with nanoparticles was assessed by rheological characterisation. Then, mechanical properties of hydrogels were controlled to match the properties of soft tissues (e.g. breast tissue). The therapeutic efficacy of 3D printed and nanoparticle-loaded hydrogels at a known dose of hydroxyl-FK866 was assessed using human breast cancer MDA-MB-231 cells. Results confirmed the expected cytotoxicity, showing approx. 52% toxicity of the hydrogel loaded, after 48 hours of incubation, whereas lower viability (approx. 36%) was measured in cells treated with free nanoparticles (control).
These findings demonstrate the value of natural-based biomaterials and nanotechnologies; this approach together with data-informed manufacturing lays the groundwork for scalable, sustainable-by-design manufacturing for next-generation bioengineered therapeutics.

KEYNOTE LECTURES - Session 13
JULIO SAN ROMAN SESSION

Bioengineered hydrogels for Regenerative Medicine

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Hydrogels, highly hydrated cross-linked polymer networks, have emerged as powerful synthetic analogs of extracellular matrices for basic cell studies as well as promising biomaterials for regenerative medicine applications. A critical advantage of these synthetic matrices over natural networks is that bioactive functionalities, such as cell adhesive sequences and growth factors, can be incorporated in precise densities while the substrate mechanical properties are independently controlled. We have engineered poly(ethylene glycol) [PEG]-maleimide hydrogels for local delivery of therapeutic proteins and cells in several regenerative medicine applications. For example, synthetic hydrogels with optimal biochemical and biophysical properties have been engineered to direct human stem cell-derived intestinal organoid growth and differentiation, and these biomaterials serve as injectable delivery vehicles that promote organoid engraftment and repair of intestinal wounds. In another application, hydrogels presenting immunomodulatory proteins induce immune acceptance of allogeneic pancreatic islets and reverse hyperglycemia in models of type 1 diabetes. These studies establish these biofunctional hydrogels as promising platforms for basic science studies and biomaterial carriers for cell delivery, engraftment and enhanced tissue repair.

Stimulating bone regeneration and vascularisation: Poly(Vinyl Alcohol) hydrogel-mineral composites

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The restoration of bone defects in the oral maxillofacial region remains a considerable challenge due to the complex anatomy and functional requirements. Synthetic substitutes have enabled substitution of autogenous grafts to an extent, however lack of vascularisation in both acellular and cell-based scaffolds, variable degradation rates, surgical manipulation and clinical performance are some of the barriers towards successful clinical translation.
Designing of scaffolds for bone tissue requires careful consideration of multiple factors to ensure optimal functionality and biocompatibility. The main considerations for designing scaffolds in this study were scaffold spatial integrity, fluid transport throughout the construct, clinical handling and malleability for surgical manipulation to fit complex anatomical bone defects. This presentation will reflect on the development of innovative three-dimensional porous hydrogel composites composed of metastable phases of calcium phosphate (CMP) and calcium carbonate with poly(vinyl alcohol) (PVA) and highlight the effect of the calcium metaphosphate and vaterite as fillers. Furthermore, embedding of magnetic nanoparticles (MNPs) on the osteogenic and angiogenic responses in vitro will be discussed.
The CMP-PVA and Vaterite-PVA yielded 3D porous elastic scaffolds resembling 'spongy bone' with fluid absorbing and versatile properties, enabling them to transport gases and nutrients across the construct, incorporate biofunctional agents and be easily shaped manually with simple tools to fit various anatomical complex bone defects.
The PVA-Vaterite with magnetic nanoparticles (MNP) scaffolds exhibited magnetic fields as expected whilst the interaction of PVA-MNP limited chain mobility of PVA thereby lowering the volume of amorphous regions in the matrix leading to a higher crosslinking density, consequently enhancing the mechanical properties without compromising the porosity. In vitro studies demonstrated that the presence of MNPs significantly improved cell adhesion, proliferation, biomineralization and additionally promoted osteogenic differentiation and enhanced endothelial cell-mediated angiogenesis under simulated physiological conditions. Thus, these scaffolds exhibit promising potential for clinical translation in oral and maxillofacial bone regeneration.

Engineering of in vitro 3D bone tissue models via Bioprinting technologies

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The development of in vitro 3D models for bone tissue has emerged as a promising approach for drug screening and the advancement of personalized medicine. These models enable drug testing on constructs fabricated with patient-derived cells, offering a more accurate and individualized platform for evaluating therapeutic interventions. This innovation has the potential to improve treatment precision and efficacy, while reducing the need for animal testing and advancing the field of personalized healthcare. In the last decade, advancements in 3D printing technologies have significantly enhanced the development of biomaterials for tissue engineering. Notably, the use of biodegradable polymers like polylactic acid (PLA) has gained attention for its versatility in creating scaffolds with controlled degradation rates, even incorporating bioceramic compounds aimed at mimicking the composition of bone tissue. Additionally, the bioprinting of hydrogels based on natural polymers such as alginates, gelatin, and collagen has opened new possibilities for replicating the extracellular matrix, which is crucial for supporting cell growth and differentiation. Moreover, the combination of these materials enables the creation of scaffolds that integrate the mechanical properties of hybrid organic-inorganic constructs with the biological cues provided by natural hydrogels, offering the potential to incorporate drugs and even cells, making it a promising approach for developing more functional and biocompatible bone tissue constructs. In this work, we present the development of scaffolds based on polylactic acid (PLA) and hydroxyapatite (HA), fabricated by 3D printing. These scaffolds were designed with different geometries, porosity, and compositions to evaluate their performance for bone tissue engineering applications. The mechanical and physicochemical properties, as well as the biological response, have been evaluated to determine their suitability for supporting cellular growth. In addition, we present preliminary results from two ongoing approaches. The first involves the development of in vitro 3D model by combining the printed scaffolds with alginate and/or gelatin hydrogels to support cell growth. These constructs are integrated into microfluidic devices with the aim of creating a platform suitable for personalized drug screening. The second approach focuses on the development of a 3D in vitro model of joint degradation, based on the formation of spheroids by culturing monocytes and fibroblasts like synoviocytes from patients with rheumatoid arthritis in Matrigel. In this model, monocytes differentiate into osteoclasts and express osteoclastogenic (RANK, OSCAR, DC-STAMP) and inflammatory (IL-6, IL-8) markers, providing a promising strategy for studying inflammatory and tissue degrading processes related to joint diseases.

Engineering cell-Instructive 3D Scaffolds via laser surface microstructuring

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While biochemical cues have long dominated tissue engineering strategies, the influence of physical properties, particularly surface microfeatures, on cell behavior is increasingly recognized. Features such as microgrooves and pits can direct cell morphology, alignment, proliferation, and differentiation. However, translating precise surface patterning to 3D scaffolds remains a significant challenge. In this work, we present a novel method that combines 3D printing with femtosecond laser micromachining to introduce well-defined microtopographies onto poly-ε-caprolactone (PCL) scaffolds. Scaffolds were fabricated layer-by-layer and then engraved in situ with controlled surface patterns (10 or 80 µm microgrooves and micropits). This integrated process enabled high-resolution, reproducible surface modification throughout the scaffold architecture. Comprehensive characterization via scanning electron microscopy, confocal imaging, and microCT confirmed the fidelity of the laser-engraved features. In vitro studies with mesenchymal stem cells (MSCs), fibroblasts, and preosteoblasts revealed enhanced cell attachment on patterned surfaces. Microgrooves promoted contact guidance and alignment in MSCs and fibroblasts, while micropatterning supported osteogenic differentiation in preosteoblasts. These results highlight the potential of surface micropatterning to modulate cell-scaffold interactions and advance the design of functional biomaterials for regenerative medicine.

Ternary multilayer systems for programming cell behaviour

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Polyelectrolyte multilayer systems (PEMS) have been studied to make coatings on implant materials and tissue engineering scaffolds but also to generate free standing films useful as wound dressings or capsules for making tissue-like constructs. So far, the huge potential of PEMS for the application in the medical field has not been fully exploited also because of technical difficulties to apply the technique to a larger scale at low cost. Indeed, the multifunctionality of such PEMS regarding the presentation of chemical cues by specific biomolecules (e.g. glycosaminoglycans, matrix proteins and cytokines) and mechanical cues achieved by controlling water content or different techniques of cross-linking has not been fully appreciated. Indeed, another potential of such PEM coatings, capsules and free-standing films is their use as systems for release of bioactive substances that provide additional tools for manipulating cell and tissue behaviour in different directions such as cell migration and growth that are essential process in wound healing requiring regeneration of dermis and epidermis, but also for directing cell differentiation. The latter can be achieved not only by application of growth factors but also in situ transfection of cells or simply by release of other essential factors promoting differentiation of stem cells towards lineages required for regeneration of specific tissues.
We will present examples from previous studies to illustrate the potential of PEMS for medical applications. We have found that the composition and cross-linking techniques affect the release of growth factor FGF-2 which promotes migration and growth of fibroblasts that play a crucial role in wound healing processes[1, 2]. Another example shows how a specific intrinsic cross-linking technique can control the release of the growth factor BMP-2 and subsequent osteogenic differentiation of mesenchymal stem cells[3]. Moreover, chemical cues based on the composition of multilayers can be combined with nanoparticles to release chemical substances or nucleic acids to achieve differentiation of stem cells or control inflammatory responses[4,5,6]. Techniques like robot dip coaters[1] or spray coating techniques are available for upscaling the multilayer film formation which should pave the way for upscaling and future medical applications[7].

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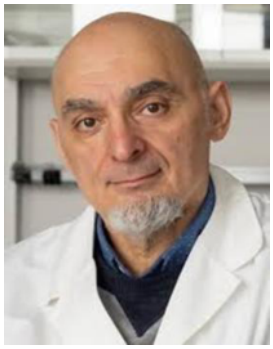
KEYNOTE LECTURES - Session 14
JULIO SAN ROMAN SESSION



Engineering Complex Coacervation to Obtain Functional Biomolecular Condensates Through Recombinant Polypeptides

José Carlos Rodríguez-Cabello

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Biomolecular condensates are unique structures formed in living cells via liquid-liquid phase separation (LLPS), primarily driven by intrinsically disordered proteins (IDPs). These proteins regulate biological functions by reversibly compartmentalizing molecules in response to stimuli. Synthetic condensate engineering seeks to design novel condensates by understanding how amino acid sequences affect the assembly and mechanical properties of IDPs. Intrinsically disordered protein polymers (IDPPs) with a lower critical solution temperature (LCST) are often used for this purpose.

This study explores synthetic condensate formation using elastin-like recombinamers (ELRs), focusing on the forces driving their coacervation: hydrophobic (simple) and electrostatic (complex) interactions at inter- and intramolecular levels. A library of IDPPs based on motifs from tropoelastin's disordered regions was recombinantly produced. It includes two highly charged monoblocks (Glu- or Lys-rich), a diblock combining both, and two hydrophobic controls with VPGVG domains of different lengths. The latter three retained elastin-like reversible inverse temperature transition (ITT) behavior and exhibited conformations similar to tropoelastin. In contrast, the charged monoblocks alone did not coacervate.

However, mixing the charged monoblocks induced complex coacervation. As the molar ratio approached charge neutrality, the transition temperatures decreased, and β-turn structures increased, as shown by DSC, ITC, circular dichroism, and molecular dynamics. Combined electrostatic and hydrophobic interactions led to higher-order conformations, with the diblock forming a more ordered structure and a lower Tt than the monoblock mixture.

Coacervation was visualized in bulk and in protocells confined within microfluidic devices. Optical and confocal microscopy revealed how tuning IDPP chains influences coacervate formation and emphasized the importance of inter- and intramolecular interactions. These methods also provided insight into the dynamic behavior of the forming structures.

Overall, our results highlight how the interplay of self-organizing forces enables complex hierarchical assemblies from IDPs. By fine-tuning electrostatic interactions, we can control the formation and maturation of protein condensates, advancing our understanding of LLPS and enabling the design of organelle-like structures with broad synthetic biology applications.

Self-assembled nano-drug delivery systems

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Different nanotechnology platforms have been developed to improve the performance of drugs. Self-assembled polymeric nanoparticles produced by the spontaneous aggregation of amphiphilic block and graft copolymers in water emerged as one of the most versatile strategies to encapsulate and deliver hydrophobic small-molecule ones owing their high chemical flexibility and modularity to tailor the nanoparticle "building blocks" and their size, hydrophilic-lipophilic balance, and surface properties. We pioneered the use of these nanoparticles for mucosal drug delivery and the active targeting of solid pediatric tumors and the central nervous system. More recently, we introduced a double self-assembly strategy in a microfluidics setup to control better nanoparticle formation and encapsulate small nucleic acids. In this talk, I will overview the different synthetic strategies we use to design self-assembled nano-drug delivery systems for passive and active drug targeting and discuss their clinical potential for the targeting of small-molecule and biological drugs. Finally, I will describe a novel nanoformulation used for the nose-to-brain delivery of cannabidiol in a rodent model of autism spectrum disorder with promising clinical potential.

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Multiresponsive polymer nanoparticles for mucosal drug delivery

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Mucus presents a major barrier for drug delivery to lungs and other mucosal tissues. Recently, materials containing thiol groups have gained attention for their ability to bypass mucosal clearance, facilitating drug delivery to the submucosal layers (Current drug delivery 15 (2018), 1087-1099). While most studies have focused on free thiol-bearing materials, disulfides and thiols exist in a dynamic equilibrium in aqueous environments, allowing for the presence of free thiols even in disulfide-containing materials (Journal of Controlled Release 294 (2019), 355-371). This study introduces a novel approach using stimuli responsive nanogels (NGs) designed with multifunctional, temperature-, pH-, and redox-responsive characteristics to enhance the mucosal delivery of small drug molecules and therapeutic biomacromolecules. We developed disulfide-bearing NGs that target the challenges of mucosal drug delivery. A thorough screening of monomers and crosslinkers was conducted to optimize the arrangement of disulfide linkers within the NG structure. We evaluated the NGs' interactions with mucus and their ability to penetrate mucosal barriers using gastrointestinal mucus from porcine small intestines and reconstructed human bronchial epithelium models. The NGs were loaded with proteins as model drugs, and their mucosal penetration was tested in three-dimensional human models and in C. elegans (Advanced Functional Materials (2024), 2407044). Our studies also demonstrated that NGs can be effective carriers for antimicrobial drugs, highlighting their interaction with mucin to target bacteria-infected mucosa (Biomacromolecules 25 (2024), 5968–5978). Moreover, the concept was further developed to decorate drug nanocrystals, enabling the delivery of highly hydrophobic drugs through the mucosa (ACS Applied Materials and Interfaces 16 (2024), 47124–47136).
Results indicated that the inclusion of disulfide bonds not only facilitates cargo release but also enhances mucoadhesion and mucopenetration. In addition, the different functional groups in the NG surface affected cargo penetration across the mucosal barrier. Future research aims to explore applications against cystic fibrosis, bovine mastitis, pneumonia, and Chagas disease.

Innovative hydrogel platforms for controlled release in Regenerative Medicine

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The therapeutic potential of mesenchymal stem cells (hMSCs) for the treatment of chronic and degenerative diseases is unquestionable. However, their clinical efficacy is limited by poor homing capacity and by local formulations that scarcely ensure cell viability or functional integration. In this context, we developed an injectable system based on aldehyde-functionalized hyaluronic acid (AHA) and O'-carboxymethyl chitosan (OCC), capable of forming hydrogels in situ and enabling controlled release of hMSCs and osteogenic factors such as BMP-2. Formulations with different degrees of functionalization (25% and 50%) exhibited distinct mechanical properties that significantly influenced the cellular response: higher stiffness and stability in AHA-50, and more favorable stress relaxation in AHA-25. Cells showed high viability in both systems, but enhanced proliferation and metabolic activity in the softer hydrogels. Taking advantage of these complementary features, we combined the rapid release of hMSCs from F-25 with the sustained delivery of BMP-2 from F-50, resulting in active osteogenic differentiation, as evidenced by increased ALP activity and nuclear Runx2 expression. These findings highlight the potential of AHA-OCC systems as versatile platforms for advanced cell therapies, capable of finely modulating both the mechanical microenvironment and the biochemical signaling required for effective tissue regeneration.

Biomaterials at the frontier of biomedical innovation: A legacy of scientific excellence and translational impact

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The development of a research career is profoundly influenced by the presence of inspiring mentors. Prof. Julio San Román, honored at this congress, has been instrumental in shaping the scientific identity of the Biomaterials Group at the Institute of Polymer Science and Technology (ICTP-CSIC). His profound expertise in polymer science including synthesis (with particular mastery of radical polymerization), chemical modification, and advanced characterization techniques, established a robust foundation for a research strategy that merges frontier fundamental science with real-world applications. His deep curiosity about medical challenges, combined with exceptional interpersonal skills, enabled him to build strong relationships with leading professionals in the biomedical field, fostering collaborations (including Prof. Allan Hoffman) that enriched the group's scientific vision and addressed complex clinical needs. Today, the Biomaterials Group, that I have the honor to lead, main research lines include: (1) nanostructured functional polymers; (2) hydrogels for advanced applications; and (3) the encapsulation and controlled release of bioactive molecules. In this presentation, I will highlight representative examples from these three research lines including a radiopaque embolic liquid currently in Phase II clinical trials; viscosupplements for the treatment of osteoarthritis; and anti-inflammatory nanoparticles for mitigating radiation-induced damage in cancer therapy. These case studies reflect our commitment to translational research based on strong scientific foundations.

KEYNOTE LECTURES - Session 15

Title: To be announced

Helen Lu

Columbia University, USA

Abstract

Acknowledgements:

Biofunctional nanostructured biomaterials aiming target therapies

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Biomaterials have been structured as nanoscale entities (e.g. nanofibers and nanoparticles) capable of interacting with biological systems at the cellular level. These nanostructures are being explored in a variety of biomedical applications such as in vitro diagnosis, in vivo imaging, drug delivery and tissue regeneration. To overcome shortcomings of nanostructured systems (e.g. limited bioactivity and suboptimal integration with the host tissue), biomolecular modification was performed to control cellular processes such as proliferation, migration, differentiation, maturation or even apoptosis. To mimic the structural function of extracellular matrix (ECM), nanofibrous meshes (NFMs) have been produced by the electrospinning technique. Despite the physical resemblance, the ability of natural ECM to locally bind, store and deliver bioactive factors to adjacent cells have been also considered. Materializing, tissue-specific proteins [1], growth factors [2] or extracellular vesicles [3] present in biological fluids were immobilized and made available at the surface of electrospun NFMs. These biofunctional nanofibrous systems were developed to specifically regenerate cartilage, bone, vascular, neural and thymic tissues, using endogenous biomolecules. In an innovative approach, polymeric nanostructures were functionalized with antibodies able to capture pro-inflammatory cytokines (i.e. TNF-alpha and IL-6) present in inflamed joints, without affecting the cellular performance of articular chondrocytes [4]. By using this approach, the neutralizing antibodies had a maximum therapeutic efficacy, reducing the severe side effects associated with their systemic administration, and avoiding the progression of inflammatory arthritic diseases. In a different attempt, nanostructures were functionalized with marine-origin bioactive compounds to differentially target melanoma [5] and breast cancer (primary and metastatic) [6] without affecting surrounding healthy cells/tissues. This selective behavior allows defining effective antitumor approaches, avoiding the side effects of current chemotherapeutics. The safety and efficacy demonstrated by these biofunctionalization strategies of nanostructured biomaterials support the development, at the preclinical stage, of advanced target therapies for impactful human health conditions.

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Polymeric and lipid-polymer drug delivery systems for cell-specific modulation in musculoskeletal disorders

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The development of innovative drug delivery systems offers a versatile approach for the treatment of musculoskeletal diseases, enabling the controlled and cell-specific administration of therapeutic agents while minimizing systemic exposure. Through the rational design of polymeric and lipid-polymer platforms, ranging from microparticles to nanostructures, we developed and characterized targeted therapeutic strategies capable of modulating cellular senescence, bone resorption, and osteogenic differentiation of mesenchymal stem cells (MSCs) with high spatial and cellular specificity.

The accumulation of chondrocytes depicting senescence-associated secretory phenotypes contribute to extracellular matrix degradation and chronic inflammation in osteoarthritis. To address this issue, polymeric microparticles encapsulating a senolytic compound were designed through AI approaches. These systems exhibited physicochemical properties suitable for intra-articular administration, including appropriate particle size and high encapsulation efficiency. In vitro assays demonstrated a reduction in senescence markers, supporting the potential of localized senescence-targeted therapy. Moreover, in vivo experiments proved a decrease in the disease progression for animals treated with the developed formulations.

On the other hand, osteoporosis is characterized by a pathological increase in osteoclast-mediated bone resorption, which exceeds osteoblastic bone formation, thereby disrupting the equilibrium of bone remodeling. Two complementary strategies were pursued in the context of this pathology. First, lipid-polymer hybrid nanoparticles were designed to deliver interleukin-4 (IL-4) to osteoclasts, aiming to inhibit their differentiation and resorptive activity. The nanoparticles functionalization enabled selective targeting of CD206-expressing cells. The resulting systems displayed a core-shell architecture, high protein encapsulation efficiency, and enhanced cellular uptake. Moreover, these systems efficiently modified the secretory profile of osteoclasts, indicating their suitability for receptor-mediated modulation of resorption activity.

Second, a systemic strategy was developed to promote osteogenesis by silencing the Wnt pathway antagonist Sfrp-1 in MSCs. This approach was selected based on the osteogenic potential of the canonical Wnt/ß-catenin pathway stimulation. Lipid-polymer nanoparticles were functionalized with an MSC-specific aptamer and loaded with a GapmeR oligonucleotide targeting SFRP1. These systems maintained favorable physicochemical characteristics and demonstrated efficient gene silencing in vitro. Their in vivo administration in osteoporotic models resulted in increased bone accumulation, reduced hepatic uptake, and significant improvements in bone microarchitecture and osteogenic marker expression.

Collectively, these findings demonstrate the versatility of polymeric delivery systems in addressing diverse therapeutic targets within the musculoskeletal environment. By integrating drug encapsulation, surface functionalization, and cell-specific targeting, these platforms constitute advanced therapeutic strategies with enhanced efficacy and safety profiles.

Exploring light-based biofabrication of norbornene-functionalized polymers for recreation of cell microenvironments

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This talk will describe two polymer systems which have been functionalized with norbornene groups to enable hydrogel formation via thiol-ene chemistry. For both systems, an all-in-one pot approach was used to form the hydrogels in cell-permissive conditions. Peptide sequences cleavable by cell-secreted matrix metalloproteinases flanked by cysteines were used as cross-linkers. Polymers were rendered cell adhesive by binding of cysteine-terminated RGD sequences. Cell were included to the mix. LAP was used as photoinitiator, and pre-gel solution exposed to 30 seconds of UV light to induce cross-linking.
The first system is based on naturally-derived polysaccharide alginate. By tuning polymer and cross-linker concentrations a stiffness range between 300 to 2100 Pa was achieved. Full cross-linking occured at 12 seconds post UV irradiation, as determined by photorheometry. Scanning electron microscopy showed a highly porous ultrastructure. Hydrogels degraded upon exposure to exogenous collagenase. Pre-gel solutions could be successfully bioprinted with a pneumatic extrusion-based system. A variety of delicate cell types were encapsulated in the hydrogels. Human endometrial organoids presented high cell viability, grew in size over time, presented spherical morphology, and expressed cell-cell contacts E-cadherin and proliferation marker ki67. Encapsulated mouse embryonic stem cell-derived thyroid follicles produced thyroglobulin and T4. Mouse intestinal organoids adopted a proliferative phenotype. Vascularization inside the hydrogels was achieved using endothelial cells and supporting cells (single cell suspension and spheroids). Neurite outgrowth, both small and thick bundles, from encapsulated iPSC-derived neurospheres demonstrated the hydrogel's reinnervation potential.
The second system is based on synthetic polyvinyl alcohol (PVA). PVA is water soluble, biocompatible, has good mechanical properties and is highly amenable to chemical modifications. At 5% w/v hydrogels had a stiffness of approximately 2000 Pa. Exogenous collagenase degraded hydrogels cross-linked with MMP, but not when PEG was used. Dermal fibroblasts were encapsulated and presented elongated and spread morphology. Granular hydrogels were obtained upon secondary cross-linking of packed hydrogel particles formed by extrusion fragmentation and by emulsion in silicon oil. Fibroblasts could attach onto the surface of the hydrogel particles and migrate through the microporous structure. Future work will focus on studying the influence of inter-particle crosslinking on cell behavior, and the biofabrication of hierarchical constructs using granular hydrogels.
These two polymer platforms allow high tunability of mechanical and biological properties to tailor the needs of cell culture, which could be an alternative to basement-membrane extracts.

KEYNOTE LECTURES - Session 16

Marine-origin biopolymers as constitutive elements of biomaterials: a blue biotechnology contribution to advanced therapies

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Blue bioeconomy is gaining a pivotal role in policies worldwide and in society at large, acknowledging the raising awareness of the effect of the Ocean in the complex architecture of life at many different levels. One of the vectors being explored regards strategies to sustainably explore marine biological resources – blue natural capital – as raw-materials for different areas. In healthcare, alternatives to petrochemical-derived polymers and to mammal-derived materials are being sought, aiming the establishment of greener, safer and ethically compliant solutions. Marine-origin biopolymers, as chitosan, alginates, seaweed sulfated polysaccharides and fish collagens are at the forefront to respond to this scientific challenge. Indeed, these molecular entities exhibit similarities with components of the native human extracellular matrix, can be produced with high purity originating from resources with no risk of posing diseases to humans nor raising ethical or religious concerns that may represent a regulatory burden. During this talk, examples of extraction methodologies applied to underexplored raw-materials, as some macroalgae, certain invertebrates and by-products resulting from industrial fish processing will be discussed. Further, several processing technologies that have been explored by 3B's Research Group to develop new biomaterials prototypes composed by these marine-origin functional units will be presented, from freeze-drying and ion gelation to (photo)crosslinking and 3D bioprinting, among others. In particular, composite porous structures of fish collagen and calcium phosphates were proposed for bone regeneration, while the blending of jellyfish collagen, squid chitosan and brown seaweed fucoidan, subsequently plastic compressed, resulted in electrostatically assembled hydrogels capable to encapsulate cells towards cartilage engineering. Fish collagen was used to prepare membranes supporting the growth of skin cells for wound healing, whereas hydrogels enriched with ascorbic acid can be seeded with keratocytes envisaging artificial corneas. Likewise, alginate and fucoidan capsules were capable to encapsulate functional pancreatic islets with reduced oxidative stress. Chitosan/fucoidan nanoparticles functionalized with selected antibodies could target specifically breast tumor cells for the sustained delivery of antitumor drug, resulting in less metastasis occurrences, whilst specific fucoidan was used as bioactive agent grafted in nanofibrous meshes to tackle melanoma. Altogether, the presented research underpins the value of marine-origin biopolymers in biomedical arena, with current impact in healthcare and promising new solutions for precision medicine towards healthier aging, in alignment with UN 2030 SDGs.

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ORAL PRESENTATIONS – Session 4

O1

Multifunctional nanoparticles for tracking Encephalitogenic Cells in a multiple sclerosis model

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Multimodal imaging platforms offer significant promise in biomedical applications, particularly for real-time tracking and diagnosis of diseases such as multiple sclerosis (MS). In this study, we present the development of a novel multifunctional nanoparticle (NP) system based on chitosan-palmitic acid (Ch/PA) conjugates for the dual-purpose imaging and tracking of encephalitogenic cells (EC) in an adoptive transfer experimental autoimmune encephalomyelitis (at-EAE) model. The NPs are engineered to encapsulate the near-infrared dye IR-820 and an alginate-stabilized ferrofluid (A-FF), providing complementary imaging modalities via near-infrared fluorescence (NIR) and magnetic resonance imaging (MRI). This NP were synthesized by ionic gelation and characterized through SEM, Cryo-TEM, zeta potential, and ICP-OES. The NPs demonstrated favorable size (40–70 nm), stability, and efficient photothermal response under NIR irradiation. Internalization studies confirmed effective uptake of NPs by ECs without inducing cytotoxicity or compromising metabolic activity. Flow cytometry and confocal microscopy showed strong and persistent intracellular fluorescence signals for up to 96 hours post-treatment. To evaluate in vivo applicability, labeled ECs were injected into C57BL/6 mice to induce at-EAE. The biodistribution of ECs was tracked through both MRI and ex vivo fluorescence microscopy. Signal localization in key CNS regions (spinal cord, brain, ganglia) was confirmed during the initial 3 days post-injection, aligning with the critical window of disease onset. Notably, the NP treatment did not alter the clinical course of at-EAE, validating their biocompatibility and non-interference with disease progression. This study demonstrates that these NPs serve as an effective tool for short-term in vivo tracking of ECs, aiding in the investigation of cellular dynamics in MS-like disease models. The dual imaging capacity, high photothermal efficiency, and minimal cytotoxicity highlight their potential as a robust platform for future theranostic applications in neuroinflammation and autoimmune disorders.

O2

Altered interaction between stem cells and collagen in an oxidative environment

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In regenerative medicine, understanding how stem cells interact with their microenvironment—particularly the extracellular matrix (ECM)—is crucial for optimizing therapeutic applications. Among ECM components, collagen plays a fundamental role, serving as both a structural scaffold and as a biochemical signaling platform that influences mesenchymal stem cell (MSC) adhesion, migration, and differentiation. The oxidation of collagen introduces various chemical modifications that may alter its biomechanical properties, affecting stem cell behavior. Therefore, further exploration of MSC behavior on oxidized collagen is crucial for advancing regenerative therapies and enhancing our understanding of pathological mechanisms associated with diabetes, cancer, and aging. To explore the effects of oxidative environments, we examined human adipose tissue-derived mesenchymal stem cells (ADMSCs) and revealed morphological and quantitative evidence of significantly altered early mechanotransduction when ADMSCs adhered to oxidized collagen (Col-Oxi). These changes impacted both focal adhesion (FA) formation and YAP/TAZ signaling pathways. Morphological observations showed that ADMSCs spread more effectively within two hours of adhesion on native collagen (Col) but exhibited a rounded morphology on Col-Oxi. This behavior correlated with reduced actin cytoskeleton development and impaired FA formation, quantitatively assessed via morphometric analysis in ImageJ. Immunofluorescence analysis further highlighted that collagen oxidation disrupted the cytosolic-to-nuclear ratio of YAP/TAZ activity, with YAP/TAZ primarily localized in the nucleus on native collagen but remaining in the cytosol on Col-Oxi, suggesting compromised signal transduction to the nucleus. Atomic Force Microscopy (AFM) analysis revealed notable structural differences. While native collagen formed relatively coarse aggregates, Col-Oxi produced much finer structures, reflecting impaired aggregation ability. The corresponding Young's moduli, however, surprisingly showed only slight changes in the viscoelastic properties and thus could not account for the observed biological disparities. Instead, oxidation-induced strong alteration in the protein layer roughness emerged as the most significant factor, with roughness decreasing dramatically from RMS 27.95 ± 5.1 nm for native Col to 5.51 ± 0.8 nm for Col-Oxi ($p < 0.05$). These findings suggest that topographic changes, rather than viscoelastic properties, predominantly influence ADMSC mechanotransduction in response to oxidized collagen.

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ORAL PRESENTATIONS - Session 6

O4

Engineered microcarriers for enhanced spheroid-based regeneration of diffuse cartilage lesions

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Osteoarthritis (OA) is a prevalent degenerative joint condition characterized by progressive cartilage degradation, resulting in pain and reduced mobility. Its onset often stems from cartilage defects that evolve into more extensive diffuse cartilage lesions (DCL), which are particularly difficult to treat due to cartilage's limited regenerative capacity. Mesenchymal stem cell (MSC)-based therapies offer regenerative potential; however, their efficacy is hampered by poor cell survival, inadequate retention, and mechanical stress during delivery, especially when administered as single-cell suspensions. To overcome these limitations, spheroids have gained attention as a promising 3D cell culture system that better mimics the native tissue environment, enhancing cell viability and intercellular signaling. Our study aims to improve spheroid-based therapies by developing tailored cell microcarriers that increase MSC retention and integration within cartilage defects. We engineered a click layer-by-layer (LbL) nanocoating system using elastin-like recombinamers (ELRs), recombinant protein polymers incorporating different bioactive sequences: (i) RGD motifs to promote cell adhesion, (ii) GTAR sequences cleavable by matrix metalloproteases for responsive degradation, and (iii) collagen type II and chondroitin sulfate-binding domains to enhance specificity for hyaline cartilage. The ELRs were chemically modified with azide and cyclooctyne groups, enabling their covalent assembly via click chemistry around MSC spheroids. The thickness of the coatings was characterized using scratching atomic force microscopy (AFM), while fluorescent labeling of ELRs allowed their visualization and confirmed homogeneous coverage. Nanoindentation studies revealed that the coating increased the viscoelastic properties of the spheroids, potentially contributing to improved mechanical integration within the lesion site. To evaluate functional performance, bovine osteochondral explants were used to mimic the cartilage environment. Upon coating degradation, cells were released from the spheroids and successfully migrated toward and spread across the cartilage surface, demonstrating both viability and binding capacity. These findings support the use of ELR-coated spheroids as an advanced therapeutic strategy for DCL. By improving cell retention, localization, and integration into cartilage tissue, this platform offers a promising route toward more effective and long-lasting regenerative treatments for OA and related joint pathologies. Furthermore, while focused on joint disease, this modular nanocoating technology represents a versatile platform for enhancing cell-based therapies. Its customizable bioadhesive properties and precise control over cell interactions make it a promising tool for advancing targeted and effective cell therapies.

ORAL PRESENTATIONS - Session 9

O5

Flexible and stretchable fet-type sensors based on organic and polymeric materials

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With the advent of the Internet of Things (IoT), strong demand has grown for flexible and stretchable sensors. Particularly, sensors based on molecules covering small organic molecules and polymers have recently attracted great interest due to their high potential for use in flexible, low-cost, solution-processable, large-area electronics. Functional properties of organic active layers can be tailored by rational molecular design or surface functionalization to enhance their selectivity and sensitivity. Nanoscopically engineered organic semiconducting materials have emerged as promising building blocks for high-performance flexible sensors. In this talk, the development of high-performance organic and polymeric semiconductors will be presented with viable approaches to selectively tune the dominant polarity of charge carriers and achieve efficient charge transport, which embrace the rational design of conjugated backbones, side-chain engineering, microstructural and morphological control. Unconventional organic and polymeric nanomaterials covering single-crystalline nanowires, nanoporous films, core-shell nanomaterials, multiple-patterned plasmonic nanostructures, and chiral supramolecules will be described with their applications in flexible and wearable sensors including photodetectors, chemical and biological sensors. In addition, the fundamental charge transport and photophysical phenomena of molecule-based active layers will be discussed.

O6

Rationally designed h2o2-activatable antioxidant polymer nanoparticles for diagnosis and therapy of renal ischemia/reperfusion injury

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Renal ischemia/reperfusion (IR) injury is a common pathological event that occurs when blood is resupplied to the kidney after a period of ischemia. One of key mediators of renal IR injury is the overproduction of reactive oxygen species (ROS), particularly hydrogen peroxide (H_2O_2), which drives inflammation and apoptosis. Given its central role, the overproduced H_2O_2 serves as both a therapeutic target and diagnostic biomarker of IR injury. To address this, we have developed two polymer-based nanotheranostic platforms that respond selectively to H_2O_2, enabling both real-time imaging and targeted therapy. The first system, T-pBMA, is based on arylboronate-containing poly(methacrylate) nanoparticles with excellent biocompatibility. These nanoparticles scavenge H_2O_2 and generate CO_2 bubbles to enhance ultrasound imaging. Surface medication with taurodeoxycholic acid (TUDCA) facilitates targeting to inflamed renal tissues via P-selectin. In a murine IR model, T-pBMA nanoparticles accumulated in the injured kidney, improved ultrasound contrast and significantly reduced inflammatory cytokine expression. The second system, Fu-PVU73, consists of a polymeric prodrug of urosodeoxycholic acid (UDCA) and vanillyl alcohol (VA) via a H_2O_2-cleavable peroxalate ester linkages. These nanoparticles, coated with fucoidan for inflamed kidney targeting, rapidly degrade in the presence of H_2O_2, releasing therapeutic agents and reducing oxidative stress. Fu-PVU73 nanoparticles also demonstrated high kidney accumulation and potent anti-inflammatory effects in vivo. Together, these H_2O_2-responsive nanotheranostics offer a promising platform for the dual imaging and treatment of renal IR injury. Their precise targeting, strong anti-oxidative activity and ultrasound visibility highlight their translational potential in managing IR injury and other H_2O_2-related pathologies.

O7

Understanding biophysical stimuli in three-dimensional microenvironments to enhance reprogramming efficiency toward induced pluripotency

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The cellular microenvironment plays a pivotal role in regulating stem cell behavior through dynamic cell-material interactions and mechanotransductive signaling. While three-dimensional (3D) culture systems have been extensively utilized to guide stem cell differentiation, their potential in somatic cell reprogramming remains less underexplored. In this study, we present a 3D hydrogel platform based on photo-crosslinkable hyaluronic acid (HA), designed to deliver biophysical cues that enhance the induction of pluripotency. The HA-based matrix supports cell viability and promotes key reprogramming hallmarks, including mesenchymal-to-epithelial transition, epigenetic remodeling, and activation of pluripotency-related genes. By systematically modulating hydrogel stiffness and applying low-intensity ultrasound, we observed synergistic effects that significantly elevated reprogramming efficiency. Mechanistically, engagement of HA with CD44 receptors was found to facilitate the early stages of reprogramming, while biophysical stimulation further accelerated the process. This biomaterial-driven 3D platform offers a promising strategy to improve iPSC generation through tailored microenvironmental design, highlighting its potential utility in regenerative medicine and reprogramming technologies.

O8

4D biomimetic and multi-stimuli responsive interfaces for enhanced in vitro models and regenerative medicine

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Introduction: Cellular alignment and bioelectrical stimulation play a pivotal role in various human tissues, including skeletal muscle and spinal cord. In cases of trauma or degenerative diseases, significant clinical challenges remain. Bioengineering and nanomedicine have paved the way for bioinspired and biomimetic strategies to enhance tissue regeneration and study physiological conditions/progresses in vitro as models. Our group explores novel biomaterial-based approaches leveraging bioelectricity, macromolecular crowding, and extracellular matrix (ECM) to recreate biological complexity.
Methods: Different biomaterial platforms were developed to address skeletal muscle and spinal cord diseases: an injectable magnetic hydrogel combining carrageenan or gellan gum with hyaluronic acid and collagen to modulate the aligned ECM microenvironment; a piezoelectric scaffold composed of piezoceramic particles (PZP) embedded in an egg white protein matrix, activated via ultrasound (US); a bioactive biomaterial based on carrageenan and egg white protein incorporating electromagnetic particles for wireless electrical stimulation via magnetic field (MF). The materials' mechanical properties were characterized, while in vitro studies assessed biocompatibility, cell viability, and differentiation using qPCR, Western blotting, intracellular calcium flux analysis, and immunomodulatory assessments.
Results: The developed platforms exhibited mechanical properties comparable to soft tissues (3-20 kPa), and high porosity (~80%). The injectable hydrogel proved to be an excellent solution for minimally invasive surgery, enabling aligned muscle tissue regeneration while promoting M2 macrophage activation creating a pro-regenerative environment.
The application of an external low-intensity MF (9 mT) is required for only 2 min, yet it is sufficient to generate a highly biomimetic anisotropic structure.
The piezoelectric scaffold, when stimulated by US or MF, induces mechanical deformation of the embedded particles, generating an electrical signal. This provides a novel tool for wireless electrical stimulation of cells, enhancing the differentiation of both muscle and neural cells cultured within this 3D model.
A comprehensive study of cell-material interactions demonstrates that these platforms can serve as alternative methods to animal testing, offering an advanced tool for investigating bioelectricity-driven mechanisms involved in various physiological and pathological cellular processes.
Conclusions: These biomimetic strategies offer innovative solutions for tissue regeneration and in vitro studies by integrating bioelectric stimulation and ECM mimicry. Furthermore, the incorporation of magnetoelectric particles introduces a synergistic approach for endogenous bioelectricity stimulation and as a dynamic platform for biomolecule delivery in a controlled manner.

ORAL PRESENTATIONS - Session 12

O9

Glycopeptide-based hydrogels as storage depots that promote vascularization

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Glycosaminoglycans (GAGs) is one of the most abundant class of biomolecules that constitute the extracellular matrix (ECM). They have a series of bioactivities, as for example: participation in cell-cell communication; mediation of ligand-receptor recognition (i.e., act as co-receptors); and enable long term storage of bioactive proteins maintaining them in their bioactive conformation (i.e., act as storage depots). Importantly, the vascularization of tissue engineering constructs plays a critical role in the regeneration process, as it provides oxygen and metabolites to the cellular components and remove metabolic products from the extracellular space. Herein, we designed a glycopeptide (i.e., Fmoc-FF-Glucosamine-6-sulfate) that self-assembles into nanofibers and gel under physiological conditions, mimicking the sulphated GAGs/proteoglycans present in the ECM. We hypothesize that these hydrogels can act as storage depots and promote vascularization. The selection of a sulphated monosaccharide in the design of the glycopeptide was done as it has been reported that sulphation is the main responsible for the capacity of the GAGs/proteoglycans to act as storage depots. The biocompatibility of the supramolecular hydrogels was confirmed under human dermal microvascular endothelial cell (hDMECs) cultures by live/dead staining and AlamarBlue® assays. These hydrogels were then loaded with angiogenic factors, e.g., fibroblast growth factor 2 (FGF-2) and vascular endothelial growth factor (VEGF)[2,3], at concentrations of 10 and 20 ng/mL, to promote vascularization.[1] The encapsulation of VEGF in the supramolecular hydrogels, induced microvascularization during 7 days using a combination of hDMECs and adipose-derived stromal/stem cells (hASCs) as demonstrated through the formation of capillary-like structures, validated by immunofluorescence imaging (lectin-FITC) and western blot analysis on days 4 and 7. Our results show that the proposed glycopeptide-based supramolecular hydrogel is able to capture angiogenic factors, maintain them in their bioactive conformation (as observed for sulphated GAGs in living tissues) and promote the pre-vascularization of supports for tissue engineering and regenerative medicine applications.

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O10

Bioengineered microtissue constructs for dual osteogenic and angiogenic stimulation to restore bone integrity in osteoradionecrosis

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Head and neck squamous cell carcinoma is an oral cancer with an incidence of around 6 per 100000 people worldwide and estimated to increase 47% by 2040. Treatment of these patients involves surgical excision followed by radiotherapy. Osteoradionecrosis (ORN) is a side-effect as a result of blood vessels damage that induce bone tissue devitalization. The regenerative process shall lead to new blood vessel re-establishment and bone tissue growth. The overall goal of this work is to offer an integrative therapeutic approach that associate a 3D bioconstruct based on natural polymer and piezolelectric composite nanoparticles with high porosity architecture and exceptional biological properties to provide the microenvironment for cells to self-organise as a living material and promote an effective reconstruction of the bone. Human dental follicle mesenchymal stem cells (dMSC) were isolated from dental follicles (Ethical approval: 50/CEUP/2018). A 3D biocomposite scaffold was developed based on collagen type I and nanohydroxyapatite with or not barium titanite nanoparticles (50:50% w/w) and tested for cytotoxicity and biocompatibility to dMSC to evaluate cell proliferation, migration and tissue formation. Afterwards, to produce cellular aggregates (spheroids), MSCs suspension as loaded into non-adhesive agarose micro-molds and allowed to settle. Spheroids were collected after 24h and characterized at different levels for osteogenic differentiation, extracellular matrix organization (immunostaining for Collagen type I and Fibronectin). A 3D piezoelectric biocomposite scaffold was successfully developed that allowed high MSCs viability (Alamar blue assay), cell migration (immunostaining for actin and nucleus) and growth (DNA quantification) after 14 days. Spheroids were successfully produced and the maintenance in size and viability were observed until 7 days into the molds. Mechanically, the spheroid's imbedded into the hydrogel allow their new ECM production based on Collagen I and fibronectin stains. After 24h, MSCs were able to spread out of the spheroid and reorganized covering all the scaffold structure. After 7 days, MSCs showed the ALP activity and gene expression of Osteopontin (osteogenic differentiation). This study demonstrates the value of piezoelectric stimulus in enhancing MSCs migration and proliferation within engineered constructs, providing clues to develop more robust tissue engineered scaffolds. In future work, by incorporating the MSC spheroids and endothelial cells, we move closer to provide clinically viable tissue engineering solutions to perform a patient-specific therapeutic treatment for osteoradionecrosis that certainly require a more robust vascular integration and bone tissue regeneration.

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O11

Toward microbiome models: bacteria encapsulation in interfacial polyelectrolyte complexes

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In cancer, commensal microbes modulate the immune response by in situ release of signaling molecules, which degrade potential carcinogens compounds, and by secretion of short-chain fatty acids that affect cell death and proliferation [1]. Aerobic or facultative bacteria residing in hypoxic or necrotic regions of the tumor can modulate the pH, metabolism, and immune landscape of the tumor microenvironment. Empirical evidence suggests that they affect the tumor multiresistances but the exact mechanisms are unclear. Thus, bacteria populations models are essential for revealing the involved signaling in cancer development/maintenance and exploring the therapeutic possibilities that cancer microbiome offers.
In this study, we engineered anisotropic models carrying facultative and aerobic bacteria. Gram-negative *Escherichia coli* (*E. coli*) and Gram-positive *Staphylococcus aureus* (*S. aureus*) were used for the prototype development. The bacteria were encapsulated using interfacial polyelectrolyte complexation (IPC) of extracellular matrix components [2]. Each bacterial strain (1×10^6 cells/mL) was suspended in either polyanionic hyaluronic acid (HA, 3 mg/mL) or polycationic collagen type I solution (Col, 3 mg/mL). Col and HA were set in contact to establish a stable interface and IPC fibers were drawn from the interface by pulling it into the air.
The bacterial addition to the polyelectrolytes did not compromise the IPC, except for the setup in which *S. aureus* was suspended in Col. Fibers were placed in tryptone soy agar (TSA) or in liquid tryptic soy broth (TSB) and bacterial survival was assessed by live/dead staining after 16 h at 37 °C. We observed that *E. coli* and *S. aureus* survive and proliferate only when the HA is supplemented with 0.4% glucose, evidencing the need for an additional carbon source to sustain the bacteria growth. Interestingly, live *E. coli* were observed inside the fibers, whereas *S. aureus* were found on the fiber surface.
These preliminary results provide a proof-of-concept that IPC is a feasible approach for the development of microbiome models. Further research will focus on the in vitro replication of specific cancer microbiomes colonizing the human body and the mechanisms affecting the spatial distribution of different bacterial strains in IPCs.

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O12

Engineering regenerative niches: encapsulation of stromal cells from ipsc-derived intestinal organoids in synthetic degradable microgels

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Human intestinal organoids (HIOs) derived from induced pluripotent stem cells (iPSCs) hold significant promise for regenerative medicine, particularly in promoting intestinal repair [1]. However, their differentiation and maturation typically rely on tumor-derived matrices such as Matrigel®, which hinders clinical translation. To overcome this limitation, fully synthetic matrices have been developed to enable safe and effective HIO delivery for intestinal regenerative therapies [2]. Among HIO-derived cell populations, stromal cells play a key role in tissue repair and homeostasis, yet their regenerative potential remains largely unexplored [3]. Here, we present a synthetic platform based on protease-degradable polyethylene glycol norbornene (PEG-NB) microgels, fabricated via microfluidics [4], to encapsulate stromal cells sorted from iPSC-derived HIOs. Stromal cells were isolated by dissociating HIOs into single cells and depleting EpCAM+ (CD326) epithelial cells via magnetic-activated cell sorting (MACS). The EpCAM negative fraction was enriched for stromal cells and characterized for vimentin, collagen I, and CD44 expression by immunostaining. PEG-NB microgels were fabricated via in situ photopolymerization using 6, 8, and 10 wt% macromer concentrations and VPM, a protease-sensitive peptide, as crosslinker. All microgel formulations yielded monodisperse microgels with homogeneous stromal cell encapsulation. Increasing macromer concentration resulted in higher Young's modulus, enabling tunable matrix stiffness. Encapsulated stromal cells maintained >80% viability over 21 days in culture, confirming the cytocompatibility of the synthetic delivery matrices. Upon IFN-γ stimulation, secretome of the encapsulated stromal cells was analyzed using LEGENDplex™ multiplex immunoassay, revealing matrix-dependent differences in cytokine release profiles. Ongoing studies involve RNA sequencing (RNA-seq) to assess how the stromal cell secretome influences iPSC-derived HIO monolayers under homeostatic and inflammatory conditions. These findings will provide insight into epithelial-stromal interactions and guide the development of stromal cell-based therapies for intestinal regeneration using synthetic delivery matrices and HIOs.

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POSTER PRESENTATIONS – Session 1
Core Biomaterials, Nanomedicine & Tumor Models

(0001)

Immunomodulatory activity of polycaprolactone nanofibers grafted with phosphatidylserine and arginine-glycine-aspartic acid (RGD)

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Phosphatidylserine (PS), a phospholipid with immunomodulatory properties, promotes M2 polarization of macrophages by serving as an "eat-me" signal during phagocytosis of apoptotic cells, thereby enhancing anti-inflammatory cytokine secretion and facilitating tissue regeneration. Similarly, arginine-glycine-aspartic acid (RGD) peptides are known to promote M2 macrophage polarization by mimicking the MFG-E8 molecule, which activates cellular integrins. In this study, a nanofibrous membrane composed of polycaprolactone (PCL) incorporating both PS and RGD was fabricated, and its effects on macrophage polarization and bone regeneration were evaluated using a rat calvarial defect model. Methods: To prepare the PS-RGD-PCL fibrous membrane, PCL, PS, and RGD-phosphatidylethanolamine were dissolved in a chloroform:methanol mixture and processed into electrospun fibers. Bone marrow-derived macrophages (BMDMs) were cultured on the membranes, and the expression levels of M2 markers—including arginase-1, transforming growth factor-β, and FIZZ1—were assessed using RT-qPCR to evaluate M2 polarization. For in vivo evaluation, a critical-sized calvarial defect (8 mm in diameter) was created in each rat (n = 6 per group), and the fibrous membranes were applied to the defect site. Microcomputed tomography (micro-CT) was performed at 0, 2, 4, 6, and 8 weeks post-implantation to monitor new bone formation. All animal procedures were approved by the Institutional Animal Care and Use Committee (IACUC; protocol no. SNU-240705-1-1). Results: Scanning electron microscopy (SEM) analysis confirmed that all membranes exhibited well-formed and uniform fibrous structures. The incorporation of PS significantly reduced the contact angle of the PCL membrane, suggesting that the hydrophilic phosphoserine moiety of the PS molecule was exposed on the fiber surface. BMDMs cultured on PS-RGD-PCL membranes demonstrated cell viability comparable to the control group. The PS-RGD-PCL membrane—especially at 3 mol% RGD—induced higher expression of M2 markers, highlighting its immunomodulatory potential. In the in vivo rat calvarial model, limited bone formation was observed in defects covered with the PCL-only membrane at 8 weeks post-implantation. In contrast, membranes containing PS (PS-PCL) and both PS and 3% RGD (PS-RGD(3%)-PCL) promoted significantly greater bone regeneration. Remarkably, the PS-RGD(3%)-PCL group exhibited the most substantial bone formation, with visible regeneration as early as 2 weeks and rapid defect closure by 4 weeks. Furthermore, this group showed the highest M2/M1 macrophage ratio at 1 week post-implantation, suggesting enhanced bone regeneration through M2-mediated immunomodulation. Conclusion: These findings suggest that PS- and RGD-grafted polycaprolactone membranes hold strong potential for promoting bone regeneration and may be valuable in orthopedic and dental implant applications.

(0002)

Sequential extraction of collagen and gelatin from the skins of codfish, meagre and blue shark in the perspective of application in healthcare

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The valorization of marine by-products has emerged as a sustainable strategy to obtain high-value biopolymers such as collagen and gelatin. In this study, collagen was extracted using acetic acid from the skins of two warm-water fish species (meagre and blue shark) and one cold-water species (codfish, both salted and non-salted), with subsequent extraction of gelatin from the remaining biomass, and a comparative analysis of their physicochemical properties was carried out. Collagen extraction yields varied across species, with blue shark exhibiting the highest yield (8.3%), followed by salted codfish (5.1%), meagre (4.8%), and non-salted codfish (4.5%). Rheological profiling revealed species-specific thermal responses, with meagre collagen displaying the highest viscosity across all tested temperatures and the highest denaturation temperature (30.3 °C), indicating superior thermal stability. FTIR and CD spectroscopy confirmed the preservation of the triple-helical structure in all samples, with characteristic amide bands observed, although minor wavenumber shifts suggest subtle structural differences among species. SDS-PAGE electrophoresis revealed typical collagen α1 and α2 chains along with β and γ components, with meagre and blue shark samples exhibiting cleaner profiles with fewer degradation products and slightly heavier α- chain bands thus suggesting higher molecular integrity compared to codfish-derived collagens. A comparison between salted and non-salted cod collagens revealed that salting improved extraction yield but negatively impacted rheological, thermal and structural stability, suggesting a detrimental effect over collagen integrity. Moreover, high molecular weight gelatin could be obtained from the remaining biomass of skins of all fish species, adding another level to the proposed strategy for valorization of fish by-products. Overall, these findings emphasize the impact of species origin and habitat temperature on collagen characteristics and suggest that meagre collagen holds strong potential for biomedical applications due to its favorable rheological and structural properties.

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(0003)

Bile acid-conjugated nanoparticles for enhanced gastrointestinal absorption

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The development of orally deliverable polymeric nanoparticles (NPs) remains a critical challenge due to the complex barriers within the gastrointestinal tract. This study reports a bile acid (BA)-conjugated nanoparticle (BNPs) system designed to enhance gastrointestinal absorption via transporter-mediated pathways. Fluorescently labeled, carboxylated polystyrene nanoparticles were conjugated with glycocholic acid to ensure colloidal stability and reproducibility during in vitro and in vivo evaluations. In vitro assays using SK-BR-3 cells, which express the apical sodium-dependent bile acid transporter, demonstrated that BNPs exhibited a 2.9-fold longer intracellular retention time compared to BA unconjugated NPs, suggesting engagement with distinct endocytic and trafficking routes. Furthermore, BNPs traversed Caco-2 cell monolayers without disrupting tight junction integrity, confirming a non-disruptive, transcellular uptake mechanism. In vivo studies employing intravital imaging revealed that orally administered BNPs were retained in the small intestine for at least four hours and gradually entered systemic circulation primarily via intestinal lymphatic pathways. Pharmacokinetic analysis in Sprague-Dawley rats indicated that fasting for four hours before and thirty minutes after administration significantly improved oral bioavailability (oBA) of BNPs, whereas postprandial administration markedly reduced absorption efficiency. Importantly, reduced gastrointestinal motility, achieved through anesthetic conditions, enhanced the relative oBA by up to 74%, highlighting the influence of intestinal dynamics on NP uptake. These findings suggest that conjugation of NPs with BA represents a viable strategy to exploit endogenous transport systems for oral delivery without compromising epithelial barrier integrity. Modulation of external factors such as feeding status and gastrointestinal motility can further optimize absorption. Ongoing studies aim to elucidate the molecular and cellular mechanisms underlying bile acid-mediated NP transport. The insights from this work provide a foundation for designing polymeric nanocarriers with enhanced oBA, broadening the scope of non-invasive drug delivery approaches for systemic therapy.

(0004)

Polyplex-based co-delivery of paclitaxel and mir-34a for advancing combination therapy in colorectal cancer

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Colorectal cancer remains one of the most prevalent malignancies worldwide, accounting for approximately 1.9 million new cases annually and ranking as the second leading cause of cancer-related mortality. Recent advances highlight the promise of combining chemotherapy with nucleic acid therapeutics to amplify anticancer efficacy through synergistic mechanisms. However, the development of versatile nanocarriers capable of co-delivering small molecule drugs and nucleic acids remains a key challenge. In this study, we engineered a co-delivery platform based on cholesterol-modified polyethyleneimine (C-PEI) and cholesterol-modified hyaluronic acid (C-HA) complexes to encapsulate both paclitaxel (PTX) and miR-34a. Drug-free C-PEI/C-HA polyplexes exhibited uniform nanoscale morphology and minimal cytotoxicity in human colorectal carcinoma (HCT116) cells, underscoring their biocompatibility. Fluorescence imaging confirmed efficient cytosolic delivery of the C-PEI/C-HA complexes in both murine colon carcinoma and human embryonic kidney cells. Notably, the co-loaded PTX/miR-34a/C-PEI/C-HA polyplexes demonstrated superior transfection efficiency and cellular uptake in HCT116 cells compared to single-agent formulations. This dual-delivery system significantly suppressed the expression of oncogenic targets, including Notch1, Snail1, and BCL-2, thereby inhibiting cancer cell migration and proliferation. These results suggest that Chol-PEI/Chol-HA-based polyplexes offer a promising strategy for combinational CRC therapy, leveraging targeted delivery to achieve enhanced therapeutic outcomes.

(0005)

Photo-crosslinked biodegradable adhesives inspired by diphenol crosslinking in resilin proteins

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In biomedical fields, there is a significant demand for biodegradable adhesives suitable for internal applications, such as tissue bonding, organ repair, and drug delivery. However, existing adhesives often lack sufficient biocompatibility and controlled biodegradability, making their development challenging. Inspired by the photochemical diphenol crosslinking observed in resilin proteins of dragonfly wings, we developed a bioinspired adhesive capable of biodegradation under physiological conditions. This adhesive was synthesized through UV-induced crosslinking of phenol-functionalized polymeric precursors, resulting in covalent diphenol bonds analogous to those naturally found in resilin. The resulting diphenol-based polymer network exhibited controllable biodegradation mediated by enzymatic action in physiological environments. Moreover, the mechanical and adhesive properties could be precisely adjusted by varying the crosslinking density. Thus, our proposed approach provides an effective strategy for developing biodegradable adhesives suitable for tissue engineering and various biomedical applications requiring safe and controlled degradation in vivo.

(0006)

The rise of in vitro models in investigating tumor-induced cachexia

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Tumor-induced cachexia (TiC) is a complex condition often seen in states of advanced cancer development. Far more than weight loss, it manifests as severe and progressive loss of skeletal muscle/adipose tissue and chronic inflammation, being inherently related to cancer mortality and poor prognosis (e.g., reduced treatment tolerance and impaired physical function)[1]. Due to its heterogeneity and complexity, there are currently no effective therapies for TiC[1]. To meet this challenge, researchers are turning to the lab bench. Even though TiC pre-clinical research has been mainly conducted using animal models, these still present limitations (e.g., ethical issues, high costs, subpar human-specific responses)[2]. *In vitro* models have been viewed as helpful tools for dissecting the cellular and molecular mechanisms of TiC in a more controlled and scalable environment[3]. Non-debatably, monoculture systems are the most used, with C2C12 and 3T3-L1 being the cell lines used for studying skeletal muscle wasting and adipose tissue loss, respectively. Additionally, different induction methods have been used to establish the cachexia-induced phenotype (e.g., conditioned medium, Dexamethasone, Cisplatin)[3]. Nevertheless, it is essential to move from this simpler approach and enhance physiological relevance, opting to develop co-culture systems, 3D-printable models, and organ-on-a-chip technologies. These novel approaches allow for the mimicry of complex tumor-host crosstalk, the integration of extracellular components, 3D tissue architecture, and the inclusion of biomechanical cues. In the long run, the constant improvement and standardization of these *in vitro* models provide a valuable toolkit to transform the diagnosis, drug screening, and personalized treatment strategies for TiC.

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(0007)

A multifunctional hydrogel to damage residual glioblastoma cells post-resection

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Glioblastoma (GB) is the most prevalent and lethal primary malignant brain tumor. Despite advances in surgical techniques, molecular profiling, imaging technologies, and drug development, current therapy offers only modest survival benefits, with a median patient survival of approximately 12 months. Recurrence typically occurs within or near the resection cavity, highlighting the urgent need for innovative therapies that effectively target residual tumor cells and inhibit infiltrative growth in the peritumoral region. This study presents a novel therapeutic strategy involving a hydrogel designed for in situ application immediately after maximal tumor resection. The hydrogel is composed of high molecular weight hyaluronic acid (HA) functionalized with FHKHKSPALSPVGGG, a peptide inhibitor of tenascin C (TN-C). This extracellular matrix protein is overexpressed in GB, promoting tumor invasiveness, proliferation, and resistance to therapy. By mimicking brain tissue mechanical properties, the hydrogel creates a permissive microenvironment for tumor cell attachment while neutralizing TN-C-mediated pro-tumorigenic signaling. To further stimulate tumor cell recruitment and killing, the hydrogel incorporates a chemotactic agent, 2-deoxy-D-glucose (2-DG), and large unilamellar vesicles (LUVs) loaded with docosahexaenoic acid (DHA) and doxorubicin (DOX). LUVs were synthesized using microfluidics, displaying spherical morphology, a size of ≈120 nm, a negative surface charge (≈-25 mV), and a polydispersity index of ≈0.17, confirming homogeneity. DOX and DHA were encapsulated at therapeutic concentrations, considering their IC_{50} values (≈6.3 µM and 110.8 µM, respectively, at 24 h). Their combination induced a greater reduction in GB cell viability than either agent alone, indicating a synergistic effect. The 2-DG, a glycolysis-disrupting glucose analogue, demonstrated chemotactic activity toward U87 cells, being selected at the highest concentration without cytotoxic effects (250 µM). *In vitro* assays confirmed that the TN-C inhibitor-functionalized hydrogel exhibited an anti-proliferative effect, in contrast to the non-functionalized formulation. Moreover, the final formulation—TN-C inhibitor peptide-functionalized HA hydrogel containing 2-DG and drug-loaded LUVs—showed robust efficacy against GB cells while sparing astrocytes, supporting its efficacy and safety. These results were validated using a 3D biofabricated tumor model based on hollow-fiber hydrogels to replicate the post-resection microenvironment. In this model, the multifunctional hydrogel exhibited significant cytotoxicity at 48 h, likely reflecting the kinetics of drug release and diffusion. In conclusion, this multifunctional hydrogel represents a promising localized therapeutic strategy to improve outcomes for GB patients.

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(0008)

Exploring biomaterials for pelvic organ prolapse repair: biocompatibility performance

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Pelvic organs prolapse (POP) is a pathology characterized by the descent of one or more vaginal compartments [1]. Surgical meshes are commonly used to repair POP, reinforcing the pelvic organs [2]. These meshes are typically made of polypropylene, a non-degradable polymer that can lead to complications, such erosion due to the difference in mechanical properties as compared to natural tissue [3]. In this study, we aim to explore the potential of biomaterials, such as gelatin (Gel) and alkali lignin (AL), in terms of physicochemical properties and biocompatibility, to contribute to future treatments for POP. Hydrogel membranes were prepared using GelxALy, where *x* and *y* represent the concentrations of gelatin and alkali lignin in % (w/v), respectively. Membranes were produced by mixing lignin and gelatin under controlled heating and stirring, crosslinked with genipin 0.01% (w/v), and molded in a 24-well plate for 24 hours at room temperature. Physicochemical characterization enabled to select the most promising formulation (Gel10AL5). For the *in vitro* cytotoxicity screening studies, L929 cells were seeded at the membranes surface. The results of cell viability, metabolic activity, and proliferation were analyzed after 1, 3, and 7 days of culturing. The cells morphology and attachment to the membranes surface was also investigated by scanning electron microscopy (SEM) analysis. The *in vitro* results demonstrated that gelatin-lignin membranes present promising properties for their application in the development of future POP treatments.

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(0009)

Unravelling the effects of glycated collagen on msc adhesion and mechanotransduction

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Mesenchymal stem cells (MSC) utilise collagen to restore structural integrity in damaged tissues, preserving their function. The extracellular matrix (ECM) initiates a variety of signals that activate intracellular signalling events through cell-matrix interactions. The non-enzymatic glycation of collagen, caused by hyperglycemia, can potentially disrupt MSC communication, contributing to pathologies such as diabetic complications and ageing. This study investigates the effects of in vitro glycated rat tail collagen (RTC) exposed to 0.5 M glucose for 1 or 5 days (GL1 and GL 5 respectively) on human adipose tissue-derived MSC. Early glycation of collagen leads to structural and topographical changes in the modified collagen molecules. AFM measurement revealed a more pronounced decrease in surface potential for 1-day glycated collagen (559 ± 18.4 mv) relative to native collagen (789 ± 93.7 mv). This change in surface potential indicates that glycation may alter the electrostatic properties of the collagen, potentially affecting its interactions with surrounding molecules. The surface roughness patterns were changed (Rrms varying from 3.0 ± 0.4 nm in native collagen to 2.53 ± 0.6 nm and 7.70 ± 0.6 nm in GL1 and GL5, respectively. Elasticity decreases in glycated samples as well. The Young's modulus of GL1 was found to be reduced to 6.90 ± 0.5 MPa, which is much lower (5x) than that of native collagen. The elastic modulus decreased even more for the (GL5) sample. MSC exhibit altered adhesion dynamics to glycated collagen, with significant changes in early attachment and detachment patterns, indicating impaired recognition by integrin receptors. Additionally, there is reduced fibril-like reorganisation and altered early steps of mechanotransduction, as evidenced by changes in the cytosolic-to-nuclear YAP/TAZ ratio. While the mechanisms behind these changes remain uncertain, differential scanning calorimetry suggests subtle structural and thermodynamic alterations in glycated collagen. These findings highlight the potential impact of glycation on MSC behaviour and its implications for conditions such as diabetic complications and ageing.

(0010)

Lighting up the tumor microenvironment: engineering biomedical polymer optics for next-generation living optical fibers

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Despite advances in cancer research, there is a long-standing need to improve *in vitro* models to enhance the speed and accuracy of drug studies and reveal insights into complex tumor biology. Living optical fibers have emerged as a promising response to these challenges. These structures, composed of different hydrogel layers, guide light using the same technology as traditional optical fibers [1]. Depending on cell concentration and behavior, they interact with light throughout the fiber, and variations in light intensity and specific optical fingerprints can be used to detect and analyze 3D biological events. Current limitations in the performance of these hydrogel optical fibers can be overcome by improving the refractive index (RI) of the fiber core without compromising transparency or cellular compatibility.

Herein, fibers were produced using a triaxial nozzle, obtaining a fiber with a core, a middle (cladding), and an outer (protective) layer. To optimize light propagation through the core - the light-guiding compartment - different formulations and concentrations of ionic hydrogels like alginate and gellan gum were studied. Then, we explored how the ionic crosslinking bath could be tuned to reduce fiber opacity and light guiding loss. Our tests showed that Very Low Viscosity Alginate (Pronova Up VLVM) at 5% was ideal for the core, and that combining Barium Chloride ($BaCl_2$) with Calcium Chloride ($CaCl_2$) in the crosslinking bath significantly reduced fiber opacity (6 times more transparent) while maintaining construct stability.

Cytocompatibility tests with MDA-MB-231 breast cancer cells (10×10^6 cells/mL) encapsulated in the core showed no significant differences in cell viability after 24 hours and 1 week of incubation, when compared to the control crosslinking bath ($CaCl_2$ only) or previous fiber compositions. Optical analysis demonstrated reduced light loss and better signal integrity over long distances, also with encapsulated cells. Crosslinking with the optimized bath also led to gels that are softer than those crosslinked with the control bath, and with mechanical properties closer to those of the native breast tissue stiffness (~200 Pa to 2 kPa). Our results demonstrate that optimizing optical characteristics of natural biopolymer-based hydrogels significantly enhances fiber transparency and light-guiding without compromising cellular viability, effectively setting the stage for a new generation of living optical fibers with increased capacity to digitalize complex cancer events with unprecedented sensitivity and speed.

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(0011)

Targeted restoration of tumor suppressor function of PTEN via systemic nanocomplex-mediated gene delivery

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Phosphatase and tensin homolog (PTEN) is a critical tumor suppressor antagonizing the PI3K/AKT pathway, and its loss is a hallmark of cancer progression, metastasis, and treatment resistance, highlighting the urgent need for effective restoration strategies. However, safe and targeted delivery of therapeutic genes, especially using non-viral vectors to pathological tissues and specific cell populations, remains a significant hurdle. We developed a polymer–lipid hybrid nanocomplex (PLNC) with low cytotoxicity, improved transgene expression, and disease-targeted delivery capabilities to overcome these limitations. To formulate the PLNC, we combined cationic polymer at various ratios to optimize nucleic acid encapsulation, particle characteristics, and helper lipids (DMG-PEG2000, DSPC, and cholesterol). We synthesized non-viral cationic polymers (TPCL, CPCL, and BPCL) to ensure low cytotoxicity by conjugating quaternary onium-containing molecules to a biodegradable polymer backbone. The optimal polymer composition in PLNC was selected based on gel electrophoresis and in vitro transfection efficiency in HEK293 cells using a plasmid luciferase reporter. We assessed PTEN plasmid DNA delivery in both in vitro and in vivo models using B16F10 metastatic melanoma cells to evaluate the therapeutic potential. As a result, PLNC exhibited a uniform particle size distribution, with diameters ranging from 50 to 200 nm, and tunable surface charges indicated by zeta potential measurements. Notably, PLNCs demonstrated up to a 16.6-fold higher gene transfection efficiency than conventional lipid nanoparticle formulations in HEK293 cells. While blank nanocomplexes induced minimal cytotoxicity, PTEN-loaded formulations significantly reduced the viability of metastatic cancer cells, resulting in up to 80% cell death, indicating potent therapeutic efficacy through restored PTEN function. This nanocomplex system significantly enhances the efficiency and safety of PTEN gene therapy, offering a promising new paradigm for the treatment of refractory cancers, including metastatic melanoma.

(0012)

Harnessing the paracrine power of MSCs: enhancing adipose stem cell regenerative traits using exogenous secretome

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Mesenchymal stromal cells (MSCs) are central to regenerative medicine due to their multipotency and potent paracrine activity. Increasingly, attention has shifted from cell-based therapies to the use of the MSC-derived bioactive molecules, which include a diverse array of cytokines, growth factors, and extracellular vesicles capable of modulating cell behavior. Unlike whole-cell approaches, these bioactive molecules offer low immunogenicity, no risk of uncontrolled cell growth, and greater ease of integration into biomaterials such as hydrogels, scaffolds, and coatings. These properties make it especially attractive for biomedical applications where controlled release and safety are critical. In this study, we evaluated the effects of lyophilized bioactive molecules from umbilical cord Wharton's Jelly MSCs (WJ-MSCs) on human adipose-derived MSCs (hASCs), with a focus on enhancing regenerative traits crucial for tissue engineering. The WJ-MSC bioactive molecules were provided by the company BulGen (Bulgaria), where they are isolated through culture supernatant collection, followed by dialysis and lyophilization to preserve and concentrate bioactive factors. The lyophilized product was then reconstituted and added to the culture medium and administered to hASCs. Using light microscopy, fluorescence imaging, and image-based cytometry, we evaluated changes in cell morphology, proliferation (cell doubling time), migration (*in vitro* wound healing assay), and collagen synthesis. Cell cycle progression and cell size distribution were also assessed to determine functional alterations in treated hASCs. Treatment with the WJ-MSC biomolecules resulted in accelerated proliferation, enhanced migratory capacity, and increased collagen production in hASCs—hallmarks of improved regenerative potential. Additionally, treated cells exhibited a notable increase in cell size and advancing of cell cycle phase distribution, suggesting a shift in cellular dynamics favoring active regeneration. Our findings support the utility of lyophilized MSC-derived biomolecules as a bioactive supplement to modulate and enhance the behavior of other stromal cells. This paracrine-based strategy represents a promising, cell-free approach in biomaterial-assisted tissue regeneration. Integration of MSCs' biomolecules into biopolymer scaffolds, like nanofibers or hydrogel-based delivery systems, could further localize and prolong their effects *in vivo*, opening new avenues in wound healing, soft tissue repair, and bioactive implant design.

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(0013)

Antibacterial nanoparticles based on chitosan/methacrylated hyaluronic acid for treatment of chronic wounds

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Current wound healing treatments used in clinics are based on prevention and early detection. After diagnosis, the adopted measures include cleansing and debridement, infection and inflammation control, pressure redistribution, restoration of tissue perfusion measures, and advanced cell therapies. Nonetheless, these approaches frequently fail to completely close ulcers, which can only be solved by amputations and result in a lower quality of life for patients, and in some cases, even death. Such poor clinical outcomes demonstrate that new wound healing treatments and devices are needed. In this work, we developed new natural-derived nanoparticles to impair bacterial colonization and hinder the formation of biofilms in wounds. The nanoparticles were produced through the polyelectrolyte complexation of chitosan (CS, polycation) and hyaluronic acid (HA, polyanion). UV-induced photo-crosslinking was used to enhance the stability of the nanoparticles. To achieve this, HA was methacrylated (HAMA, degree of modification of 20%). Cross-linked nanoparticles showed enhanced stability and a more homogeneous size distribution (around 478 nm) than nanoparticles assembled solely through complexation (between 742 and 769 nm). These nanoparticles were loaded with the antimicrobial agent bacitracin (BC) at 0.7 mg/mL, with an encapsulation efficiency of 97 %, and showed significant antibacterial activity against gram-positive bacteria *Staphylococcus aureus*, methicillin-resistant *S. aureus* and *Staphylococcus epidermidis*. Photo-crosslinked HAMA/CS nanoparticles loaded with BC inhibited biofilm formation and were non-cytotoxic towards L929 fibroblasts. Furthermore, DNA content and metabolic activity were increased over 3 days, indicating that the nanoparticles sustained cell proliferation. These crosslinked nanoparticles have potential for the long-term treatment of wounds and controlled antibiotic delivery at the location of a lesion.[1]

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(0014)

A light-activated antibody-polymer system for targeted cytotoxicity and immune stimulation in resistant cancers

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Resistance, to antibodies in tumors poses a significant challenge for maintaining effective long term treatment outcomes; especially when mutations in internal signaling pathways hinder the effectiveness of surface targeted medications. To address this issue effectively and improve response in cancers while reducing off target side effects, through controlled activation strategies; we have developed an antibody conjugate that merges precise cell targeting with photo-responsive cytotoxic activation using a versatile design incorporating a photosensitizer and an amphiphilic polymer linker. This engineered platform incorporates antibodies conjugated to photoreactive molecules via polymers containing both hydrophilic and hydrophobic domains. The polymer linker promotes hydrophobic interactions at the cell interface, improving solubility, reducing aggregation, and enhancing lipid membrane affinity. Photosensitizers remain pharmacologically inactive until exposed to light of a specific wavelength, allowing for externally regulated cell death with minimal systemic toxicity. This controlled local activation selectively inflicts damage within the targeted tumor microenvironment, reduces unintended effects in healthy tissue, and improves therapeutic precision. In vitro cell experiments demonstrated that the construct retained specific targeting efficacy and induced robust cellular uptake in a variety of epithelial tumor cells, including those harboring activating mutations in intracellular signaling mediators. Upon light exposure, reactive oxygen species (ROS) significantly increased, which caused local cytotoxicity. Post-treatment analysis revealed downregulation of signaling pathways, including those involving mitogen-activated kinase and phosphoinositide kinase. Transcriptome-wide analysis further revealed concurrent activation of innate immunity, inflammatory cytokine signaling, and immunogenic cell death markers. These results collectively support the synergistic mechanistic action of the platform combining direct tumor killing and immune system stimulation. In animal studies, increased tumor accumulation and prolonged systemic circulation were observed compared to non-polymer-linked analogues. After local photoactivation, treated animals showed a strong tumor growth inhibition effect, with minimal off-target effects and stable body weight. Immunological analysis showed a significant increase in mature antigen-presenting cells and effector T lymphocyte populations, while regulatory T lymphocytes were reduced. In addition, central memory markers indicating long-term immune priming were observed. Importantly, comprehensive toxicological evaluation confirmed high systemic tolerability, with no organ damage or hematological abnormalities observed. This study demonstrates that an exogenously activatable antibody conjugate can induce sustained antitumor immunity while bypassing intracellular resistance. This approach provides a flexible therapeutic platform that can integrate molecular targeting, precise activation, and immune modulation, holding promise for the treatment of refractory malignancies that are difficult to treat with conventional therapies.

(0015)

Bioengineered viscoelastic spider silk-based bilayer patch for abdominal tissue regeneration

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Current approaches fail to restore the biomechanical properties of the abdominal wall, resulting in additional regenerative problems [1]. Proteins derived from spider silk have significant potential for creating alternative structures due to their inherent biomechanical features. Spider silk proteins are structural proteins characterised by exceptional mechanical capabilities, gradual biodegradability, and enhanced biocompatibility [2]. Herein, we explored the potential of bioengineered spider silk proteins (6mer) as a component of a hybrid patch designed to promote abdominal tissue regeneration and restore tissue function. To achieve this goal, we fused specific linkage peptides to the bioengineered spider silk proteins, envisioning the creation of new modular and tuneable protein hybrids. Hydrogels were made by combining the bioengineered spider silk proteins (0.2%; 6mer-ST; 6mer-SC) with collagen type I (1.5%, Col). Their mechanical properties and rheological behaviours were evaluated. Trying to recapitulate the cellular organisation of the abdominal wall, a bilayer patch was developed that combined the functionalised hydrogel (cultured with endothelial cells) with an electrospun fibrous mesh (cultured with myoblasts). The new spider silk proteins formed a stable hybrid protein, 6mer-ST-6mer-SC, which maintained the self-assembly properties of spider silk domains. Rheology studies revealed that the hybrid protein 6mer-ST-6mer-SC presents increased viscosity compared to the individual ones, suggesting an interaction between 6mer-ST and 6mer-SC proteins. When mixed with collagen, the hydrogels made of 6mer-SC or 6mer-ST6mer-SC presented similar viscosity to the control hydrogel. The bilayer patch allowed both endothelial and myoblastic cells to grow together for up to 7 days, as shown by the viability test and the presence of specific markers for each cell type. Overall, our findings provide new understanding of how recombinant spider silk can be used and how bilayer structures can be made for the abdominal wall, helping to create the best conditions for tissue regeneration.

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(0016)

Effect of extraction conditions on the composition and bioactivity of brown seaweeds extracts

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Seaweeds are a valuable source of structurally diverse biopolymers, particularly polysaccharides, with growing interest in biomedical, nutraceutical, and cosmetic fields. Brown seaweeds, in particular, contain polysaccharides such as alginates, fucoidans, and laminarins, which have been associated with various bioactivities. The development of environmentally conscious extraction methods is essential to support the sustainable exploitation of these marine resources. This study explores the potential of two brown seaweed species: *Rugulopteryx okamurae*, an invasive species along European coasts, and *Bifurcaria bifurcata*, native to the North Atlantic. The objective was to evaluate how processing parameters influence the yield and composition of fractions, with a focus on the recovery of functional biopolymers. A pressurized hot water extraction (PHWE) approach was employed using a range of temperatures and comparing both fresh and dried biomass. Following extraction, liquid and solid fractions were separated by filtration. Alginate was selectively recovered from the liquid phase by calcium chloride precipitation. The remaining liquid extract was analyzed for protein content, carbohydrates, sulfate groups, phenolic compounds (floroglucinol), and antioxidant activity (DPPH, TEAC, FRAP). Solid fraction, representing the non-solubilized material, was retained for further compositional assessment. The results demonstrated that extraction temperature and initial biomass state significantly affected both the recovery and the biochemical profile of the extracts. The detection of sulfate groups in the alginate-free liquid fraction suggests the presence of sulfated polysaccharides. Additionally, phenolic content and antioxidant activity were found to vary with processing conditions, suggesting potential to modulate bioactive properties through tailored extraction. These findings underscore the relevance of controlled extraction strategies in the development of functional materials from marine biomass. Structural characterization of the recovered polymers is ongoing to further explore their suitability for biomedical polymer applications.

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(0017)

Targeting of hyaluronic acid based nanoparticles in 3d tumor spheroid and micro-fluidic model

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Hyaluronic acid-based nanoparticles (HyA NPs) are potential drug delivery systems in cancer therapy because of their ability to target CD44 overexpressed in tumors. The targeting ability of HyA NPs has been extensively studied in in vitro and in vivo models. In this study, HyA NPs were prepared and tumor targeting efficacy was evaluated in three dimensional (3D) tumor spheroid micro-fluidic models. This fluidic chip model is a system that can efficiently check the targeting ability by replacing the in vivo animal model. The prepared HyA NPs had a spherical shape with a diameter of about 250 nm. 3D spheroids with diameter of about 100 um were prepared and introduced into the microfluidic chip. The target efficacy of the HyA NPs in the microfluidic chip was observed with a confocal microscope, and the degree of targeting was qualified using Image J. These microfluidic chips are expected to respected to replace animal models in the future because biomimetic is better than in vitro studies.

(0018)

Click-to-print 3d gummies: a layered nanostructured lipid carrier platform for pediatric brain tumor treatment

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Pediatric brain tumors are the most common cause of cancer-related death in children. Formulation development for this population presents unique challenges, including patient heterogeneity, rapid physiological changes that affect pharmacokinetics, and the need for precise dosing. Children also often struggle with swallowing and poor compliance due to the unpleasant taste of medications. Therefore, a “one size fits all” approach is inadequate, highlighting the need for age-specific, personalized formulations with tailored delivery methods to ensure safe, effective, and acceptable therapies. This work addresses these challenges by developing 3D-extrusion-printed multilayered gummies incorporating nanostructured lipid carriers (NLCs) loaded with pimavanserin and cloxiquine, two repurposed drug candidates for pediatric brain cancer therapy. These gummies are designed to be soft, easy to administer, and palatable, masking the bitter taste of active pharmaceutical ingredients while allowing controlled and sequential drug release through their layered structure. The NLC dispersion was prepared using hot high-pressure homogenization to achieve optimal particle size, physical stability, and efficient drug loading. This dispersion also served as the hydration medium for the polymers, ensuring uniform integration of all excipients. The hydration process was performed at 50 °C overnight to achieve complete homogenization of the inks and improve their rheological properties for printing. Different gelatin concentrations (7.5%, 10%, and 12.5%) and a combination of polymers with release-modulating properties, including xanthan gum, hydroxypropyl methylcellulose (HPMC), chitosan, and low-substituted hydroxypropyl cellulose, were investigated. Rheological evaluation was conducted to optimize ink parameters, including viscosity, elasticity, and shear-thinning behavior, which are crucial for achieving high-resolution prints. Extrusion parameters, including temperature, pressure, and nozzle size, were also optimized to ensure shape fidelity and reproducibility. Among all tested formulations, only the ink containing 10% gelatin demonstrated superior printability and structural integrity, making it the most suitable candidate for gummy production. Notably, it showed no water release after fabrication (absence of syneresis). In addition to physical characterization, in vitro testing in a simulated gastrointestinal environment and kinetic drug release studies confirmed the gummies’ capacity to deliver drugs in a sustained and controlled manner. Overall, this work demonstrates the potential of 3D-extrusion printing as an innovative and child-friendly platform for producing personalized, palatable, and functional dosage forms tailored to pediatric brain oncology, with the promise of enhanced compliance and therapeutic efficacy.

(0019)

Engineering reverse thermo-responsive nanoshells

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The exceptional physicochemical properties exhibited by nanostructured materials have positioned nanotechnology as one of the most dynamic and rapidly evolving domains in science and engineering. This study reports the engineering of hollow, thermoresponsive nanostructures that undergo a sharp and reversible volumetric transition within a narrow temperature range. These architectures were synthesized via intra-micellar cross-linking of end-functionalized poly(ethylene oxide)-poly(propyleneoxide)-poly(ethyleneoxide) (PEO-PPO-PEO) dimethacrylates. The amphiphilic triblock copolymers spontaneously assemble into micelles in aqueous environments, with the hydrophobic PPO segments forming the core and the hydrophilic PEO segments forming the corona. By exploiting the micellar organization, the cross-linking reaction was confined spatially to the corona region, resulting in the formation of hollow nanoshells with PEO-rich walls. The PPO segments, while not covalently fixed, contribute to defining the hydrophobic interior domain. Upon thermal stimulation, these nanoshells exhibited a reversible expansion-contraction behavior, with volumetric changes exceeding 1300-fold, attributed to the collapse and hydration of the PEO segments around the LCST.

Two synthetic approaches—free radical polymerization and Michael addition—were employed to achieve covalent stabilization of the nanoshells. The method of cross-linking, as well as the temperature at which it was performed, significantly influenced the final morphology of the nanostructures, enabling the engineering of various shapes, including spherical and rod-like morphologies. Furthermore, the size of the nanoshells can be precisely tuned by varying the molecular weight of the triblock copolymers—for example, coupling two triblocks to increase chain length prior to cross-linking results in larger nanoshell dimensions. Additionally, in the Michael addition approach, the nanoshell size can be modulated by employing amines of different molecular weights, which affects the final nanoshell dimensions.

These thermoresponsive hollow nanostructures hold significant potential in applications such as controlled drug delivery, biosensing, and nanoreactors, where precise control over size, porosity, and thermal responsiveness is critical. Their sharp and tunable phase transition behavior, combined with structural versatility, underscores their value in the design of next-generation smart nanomaterials.

(0020)

Pulmonary surfactant-mimetic inhalable nanoparticles for targeted drug delivery and immunomodulation in lung cancer

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Lung cancer is one of the leading causes of cancer-related mortality worldwide. Chemotherapy is one of the most frequently used treatment options for lung cancer, however, it often results in significant systemic side effects and poor drug accumulation at the target lesion in the lungs. Inhalable nanomedicine has been investigated as a potential solution to these limitations. However, nanoparticle-based delivery, whether administered intravenously or via inhalation, remains limited by several challenges, including structural instability of the drug, rapid clearance by alveolar macrophages, and poor adaptation to the tumor microenvironment (TME). In this study, we designed an inhalable nanotherapeutic system designed to enhance nebulization stability and target both tumors and the TME using an exogenous pulmonary surfactant (PS), that is clinically used and easily fused with the endogenous PS layer in the alveolar space. We prepared pemetrexed-pulmonary surfactant-based nanoparticles loaded with paclitaxel (PEM-PSNP@PTX) using a self-assembly method with stirring. PEM-PSNP@PTX exhibited enhanced uptake via folate receptor targeting in both tumors and the TME, and effectively suppressed tumor growth in a mouse lung cancer model following inhalation, without any signs of in vivo toxicity. Furthermore, lung distribution analysis revealed a 20.1% decrease in CD206 expression and a 50.8% increase in CD86 expression, indicating successful polarization of M2 tumor-associated macrophages (TAMs) to the M1 TAM phenotype. These findings suggest that PEM-PSNP@PTX could enhance therapeutic outcomes by simultaneously targeting lung tumors and the TME, representing an effective therapeutic approach for lung cancer.

(0021)

Hepatocellular carcinoma-targeted drug delivery hydrogel based on boronate ester bond stability modulation

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Protocatechuic acid (PCA) shows anti-hepatocellular carcinoma (HCC) but faces clinical limitations due to short half-life and low tumor specificity. Here, we report a hydrogel (PA-CB-PCA) comprising chitosan-boronobenzoic acid (CB), protocatechualdehyde (PA), and PCA, presenting both tumor specificity and microenvironment-responsive PCA release. This property is achieved by leveraging the high expression of sialic acid (SA) in HCC cells, as well as the differential stability of boronate esters formed between SA and PCA under the weakly acidic tumor microenvironment. By grafting boronobenzoic acid onto chitosan, CB can form stable boronate ester bonds with overexpressed SA on tumor surfaces, enabling selective targeting even under mildly acidic conditions. Meanwhile, the boronic acid groups reversibly bind PCA at physiological pH, but PCA-boronate esters become labile in acidic environments, resulting in controlled PCA release in the weakly acidic tumor site. Both *in vitro* and *in vivo* evaluations demonstrate that the PA-CB-PCA hydrogel effectively suppresses tumor growth while exhibiting favorable biocompatibility, antioxidant capacity, and shear-thinning behavior, all of which highlight its promise for clinical translation. This versatile platform may also be adapted for other phenolic drugs by leveraging its tumor-targeting and microenvironment-sensitive release features. Collectively, these advantages strongly highlight the potential of the developed hydrogel system as a novel strategy for targeted therapy of hepatocellular carcinoma.

(0022)

Engineering in situ weldable vascular devices

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There are a mounting number of endoluminal devices that are currently available for minimally invasive procedures. One of the key driving forces guiding the development of new endoluminal devices is the minimization of their insertion profile, which will result in implantation procedures that are markedly less injurious to tissues and organs. Furthermore, this strategy will not only broaden the use of these devices but will also improve their clinical performance. This study introduces a strategy to markedly reduce the insertion profile of endoluminal devices by separating their components, deploying them sequentially, and rapidly and securely welding them together at their site of performance This study introduces the *in situ* welding strategy, whereby the components of the device implanted are decoupled, deployed sequentially, and rapidly and securely welded together at its site of clinical performance. This concept is illustrated here by the treatment of Abdominal Aortic Aneurysms (AAA), which are a dangerous degenerative pathology of arterial tissues, whereby the wall of the artery weakens locally and expands, often resulting in fatal vessel rupture. AAAs are currently treated with an artificial blood vessel sewn to a metallic stent (called stent-grafts) to isolate the weak vessel wall from blood flow. Aiming at overcoming the serious drawbacks of existing stent-grafts, herein we harness the *in situ* welding approach, whereby we sequentially deploy the metallic stent and then the polymeric graft, which are then welded together at the aneurysmal site. The composition of various *in situ* weldable polymers, mainly polyurethane elastomers, exhibiting the required low softening temperature and able to weld at physiologically acceptable temperatures, were fine tuned. Various expandable conduits were generated, differing in their composition, the technique used to produce them, their mechanical properties and expandability ratio. Specifically, two different types of polyurethane elastomers were used to generate both the graft and the coating of the struts of the metallic stent. The soft segment of the polyurethanes synthesized consisted of a polyether (polytetramethylene glycol) or a polyester (polycaprolactone) of different molecular weights, chain extended in all cases with hexamethylene diisocyanate (HDI), whereby polyether urethanes or polyester urethanes were formed, respectively. The two components were deployed successively in pigs, firmly *in situ* welded in less than twenty seconds, and the patency of the bi-component device was confirmed over a three-month post-implantation period.

(0023)

Synthesis of sitosterol-doxorubicin derivatives and preparation of nanoparticles for anticancer therapy

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Doxorubicin (dox) is a widely used anthracycline anticancer drug for breast cancer, lung cancer, lymphoma, digestive cancer and sarcoma. However, it has a disadvantage of fatal side effects of cardiac toxicity and short retention time. Sito-dox A and sito-dox B were synthesized as β-cytosterol-based doxorubicin derivatives, which exhibits a superior anticancer effect than doxorubicin, and a synergistic effect in combination treatment with radiation therapy Using Sito-dox A, six types of liposomes were formulated by various compositions. At the same ratio of phosphocholine and Sito-dox A, the liposomes composed of 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) were smaller than 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) liposomes. The difference between DPPC and DOPC was double bond on lipid tail that can attribute to size of liposomes. It was confirmed that liposome forms of Sito-dox A had better cytotoxicity than doxorubicin by MTT assay, and remained in cells longer than Sito-dox A by FACS analysis. As a result, these data suggest that liposomes of Sito-dox A is a good anticancer agent with reducing side effects of doxorubicin and a potential anticancer drug during radiotherapy.

(0024)

Choline-decorated polymeric nanoparticles for synergistic anticancer efficacy through enhanced drug delivery and phospholipid synthesis inhibition

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Choline (Chol) is a key bioactive substance that regulates cell proliferation, viability, and homeostasis. It is essential for synthesizing phospholipids like phosphatidylcholine, a vital component of cellular membranes and vesicles. The rapid proliferation of cancer cells increases the demand for choline uptake through choline transporters. Binding to these transporters can either inhibit or facilitate choline uptake. This study develops a strategy to block choline transporters using choline-decorated nanoparticles (NPs) to reduce choline uptake and enhance cancer cell death. The research involves synthesizing choline-decorated poly(ε-caprolactone) polymer (CholPCL-P) and preparing self-assembled nanoparticles (CholPCL-NP) using film hydration and ultrasonication. Additionally, doxorubicin (DOX) is loaded into these nanoparticles (DOX@CholPCL-NP), and its anti-cancer effects are evaluated. The combination of CholPCL-NP and DOX exhibits synergistic effects, with DOX@CholPCL-NP demonstrating significantly better anti-cancer effects than free DOX. The findings suggest that CholPCL-NPs hold potential as a promising anti-cancer nanomedicine.

Choline-PCL-Choline polymer (CholPCL-P) was synthesized by an ester conjugation between Choline and dicarboxylated PCL (PCL_{diCOOH}). Self-assembled NPs (e.g., CholPCL-NPs and DOX@CholPCL-NPs) were prepared by a three-step thin film formation, film hydration, and sonication procedure, and their sizes and zeta-potentials were evaluated. After treating the DOX-free and DOX-loaded NPs to HCT116 cells, their cell-killing effects were measured by an MTT-based cell viability method. In addition, in vivo experiments using a mouse cancer model demonstrated that treatment with CholPCL-NPs and DOX@CholPCL-NPs significantly inhibited tumor growth.

The CholPCL-P was successfully synthesized, as confirmed by ^{1}H-NMR, demonstrating the ester conjugation between choline and PCL_{diCOOH} and two choline molecules per CholPCL-P unit. Through a successive film hydration and sonication procedure, CholPCL-NPs and DOX@CholPCL-NPs were prepared in aqueous media, exhibiting average sizes of approximately 50 nm and zeta-potentials ranging from 50 to 70 mV. Notably, the treatment of HCT116 cells with CholPCL-NPs resulted in a 37% reduction in choline uptake compared to untreated cells, consequently leading to a substantial decrease in intracellular phosphatidylcholine levels. Furthermore, CholPCL-NPs alone demonstrated remarkable cell-killing effects, with an IC_{50} value of 5.8 μg/mL, unlike the negligible cytotoxicity of free choline chloride. In particular, DOX@CholPCL-NPs exhibited 10-fold better cell-killing effects than free DOX in HCT116 cells (IC_{50} values: 0.09 μg/mL versus 0.9 μg/mL). In conclusion, the designed CholPCL-NPs demonstrates potential as an anticancer nanomedicine capable of delivering therapeutic agents and disrupting choline metabolism, potentially leading to synergistic anticancer effects with other therapeutics like DOX.

(0025)

Highly sensitive mechanochromic biomedical sensor capable of identifying cancer cells' metastatic tendency

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Understanding and detecting subtle mechanical forces generated by cells, such as cellular traction forces (CTFs, ~kPa), is an important issue of interest for enhancing cancer diagnostics and advancing mechanobiology. Conventional mechanochromic organic and polymeric materials need high mechanical forces in the range of ~MPa to ~GPa to induce fluorescence changes, making them unsuitable for application in these biomedical and biological fields. In this presentation, we present a novel class of mechanochromic materials capable of responding to subtle mechanical stimuli at the cellular scale (~kPa), which has not been reported previously. Our materials undergo a mechanical force-induced phase transition, resulting in distinct and tunable fluorescence changes. Our characterization platform based on these highly sensitive mechanochromic materials effectively distinguishes subtle differences in CTF characteristics associated with the metastatic potential of cancer cells. Our platform clearly distinguishes cancer cell lines having different metastatic tendencies based on fluorescence signal turn-on rate. Furthermore, even in the application of patient-derived cancer cells (from primary tumors and metastatic sites), our platform shows a clear difference in fluorescence signal, reflecting the cancer cells' metastatic tendencies. Our mechanochromic material system is expected to provide a powerful approach for early metastasis detection and therapeutic monitoring, representing a significant advancement in mechanochromic materials for biomedical applications.

(0026)
Melt electrowriting polymers for scaffold fabrication

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Melt electrowriting (MEW) is a relatively new high-resolution 3D printing technology used to produce polymeric microfiber scaffolds with controlled fiber alignment, mechanical properties, and tailored geometries for tissue engineering (TE). A complex and multiparametric process, MEW still requires G-code generation through software ranging from open-source or proprietary software. For MEW of tubes, G-code generation in Rhinoceros and Grasshopper, enable rapid and reproducible prototyping of tubular MEW scaffolds. Open-source hardware costing as little as $1,000 can be used to perform MEW. High-precision, custom-built MEW printers can result in library of small diameter tubes with tight tolerances, i.e. fiber diameters of 10.8 ± 0.7 µm and 20.7 ± 0.9 µm printed onto mandrels as small as 1 mm in diameter. The gold standard polymer processed via MEW is medical-grade PCL. The resulting MEW scaffolds promote cell proliferation and migration of many cell types. For guided cell growth *in vitro*, both primary Schwann cells and C2C12 myoblast cell line promote cell alignment, migration and the latter differentiated towards myogenic lineage behavior. The material-cell interface can be altered via dip-coating in hydrogels, including methacrylated hyaluronic acid (MeHA) or phase-separated poly(2-hydroxyethyl methacrylate) (pHEMA). Functionalization of pHEMA coated MEW scaffolds with RGD peptide (CG-RGD-SG) increased fibroblast adhesion 2.8-fold over unmodified pHEMA ($p = 0.02$), giving a spectrum of cell adhesion outcomes. For biomaterial implants for craniofacial surgery, tubular scaffolds were fabricated to mimic the tooth root geometries in rats, leveraging the high fidelity of MEW to design and print complex 3D architectures. Emphasizing the importance of automation, a soldering iron-based perforation method SES tubular mesh design and manufacturing were enhanced through an automated. Compared to rolling flat meshes, automated perforation of SES tubes was highly reproducible, reduced fabrication time by 67%, decreased material waste decreased by 30%, and surgeon satisfaction improved with defect rates falling from 30% to none rejected. Compressive resistance matches that of manually assembled meshes, and *in vivo* studies in a rat femoral defect model showed similarly increased bone regeneration after 8 weeks. Taken together, automation processes (i.e. MEW, SES) drive the field of biofabrication, which is becoming a significant field of discovery. Increased resolutions of scaffolds give increased design space which in turn provides tailored mechanical properties and interaction with cells/tissues. Such biofabrication methods available enable scaffold designs for both *in vitro* and *in vivo* products for neural, musculoskeletal, dental, skin, and bone tissue regeneration.

(0027)

Cytotoxicity evaluation of a miniaturized flexible oxygen biosensor

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Oxygen is vital for human life, as an adequate supply is essential to meet cellular metabolic and energetic demands. Measuring dissolved oxygen in tissues is critical in biomedical fields, such as oncology, where tumor hypoxia is increasingly recognized as an unfavorable factor in cancer therapies. Consequently, developing implantable biosensors for continuous metabolite monitoring is an area of sustained scientific and technological interest. Continuous metabolic monitoring offers significant potential for early detection of various disorders and diseases. Moreover, miniaturization and the use of biocompatible, flexible materials can minimize the body's response while maintaining sensor functionality. Recently, we developed planar, miniaturized, all-solid-state Clark-type oxygen sensors using standard microfabrication processes at the wafer level. These sensors were coated with a Nafion solid polymer electrolyte membrane to ensure robustness, biocompatibility, and selectivity. The sensors were tested in the presence and absence of dissolved oxygen, yielding results comparable to those reported in the literature. To evaluate the biosensor's suitability for biomedical applications, we assessed its cytotoxicity. Extracts were prepared by exposing the biosensor to culture media for 7 and 14 days. These extracts were tested for cytotoxicity using L929 murine fibroblasts. The metabolic activity of L929 cells remained unaffected after 72 hours of incubation with the extracts. Additionally, a Live/Dead (Calcein-AM/Propidium iodide) assay showed no significant impact on cell viability. For direct cytotoxicity testing, the flattened biosensor substrate was placed in a well plate and seeded with L929 cells. After 72 hours, cell morphology was comparable to that of cells cultured on a standard culture plate. Live/Dead assays confirmed no reduction in cell viability for cells in direct contact with the biosensor. Phalloidin and DAPI staining further revealed normal cell morphology in these conditions. Collectively, these results demonstrate that the biosensor and its extracts are non-cytotoxic. Thus, this flexible, solid-state oxygen biosensor is a promising candidate for biomedical applications, including in vivo implantation, in vitro testing, and integration into microfluidic lab-on-a-chip systems.

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(0028)

Human microcirculation-on-a-chip model reveals lung cancer-driven lymphatic remodeling and invasion

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The microcirculation system is a key player in cancer progression, yet its complex cellular composition, structural organization, and dynamic functions have proven difficult to replicate in experimental models. While traditional microfluidic models of tumor microenvironments typically focus on blood vessels and use endothelial cell-coated channels, these systems fall short in mimicking physiological conditions. To overcome these limitations we developed a human microcirculation-on-a-chip model that integrates 3D self-organized blood and lymphatic microvasculature with tumor spheroids. This platform enables comprehensive investigation of the interactions between multi-cellular tumors and both vasculatures. Using lung cancer as a case study, we examined the influence of tumor-derived mediators and cellular crosstalk on vessel reorganization and invasion capacity, identifying key molecular factors involved. Our model successfully recapitulated key features of native lung tissue, rapidly forming 3D networks and expressing pulmonary-PMV and lymphatic-LMV microvessel biomarkers. Following tumor injection, PMV/LMV exhibited distinct structural alterations depending on tumor lymphangiogenic potential. Specifically, lymphangiogenic tumors promoted greater lymphatic infiltration, tumor invasion, and microvascular growth than non-lymphangiogenic cells. Biophysical analyses showed that LMV exhibited larger diameters, lengths, densities and sprouting than PMV, and that the magnitude of these parameters correlated with tumor lymphangiogenic potential. These structural differences suggested that tumor-specific secreted factors drive vessel remodeling. Cytokine analysis supported this, showing upregulation of G-CSF, IL8, IL6 and HGF, specifically in lymphangiogenic tumors. These findings indicate distinct molecular signatures associated with tumor invasiveness and lymphangiogenesis, with inflammatory mechanisms facilitating vascular remodeling in more aggressive lung cancers. A cytokine heatmap further linked specific cytokines to tumor invasiveness and vascular remodeling, pointing to potential therapeutic targets. Overall, our microcirculation-on-a-chip offers a platform to model lung cancer neo-vascularization, uncover mechanisms of vascular invasion, and support drug screening.

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(0029)

Thioketal-biopolymer systems as a platform for ROS-responsive drug delivery and regenerative applications

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Inflammatory processes driven by reactive oxygen species (ROS) significantly affect global health, contributing to conditions such as cancer, cardiovascular diseases, skin injuries, etc. These conditions demand innovative therapeutic strategies, including smart stimuli-responsive systems capable of scavenging harmful ROS while delivering therapeutic agents. One promising approach involves the incorporation of sulfur-based ROS-sensitive moieties, such as thioketals (TK), which could selectively undergo cleavage in oxidative environments, inducing a chemical change that will synergistically scavenge ROS and trigger the release of an encapsulated drug. Here, we present the development of a series of thioketal (TK) compounds bearing different terminal groups—diamino and dicarboxylic acid—and their combination with various biopolymers to create smart ROS-responsive drug delivery systems (DDS). As a result of their double-end functionality, TKs can either react with one polymer chain per molecule (functionalization) or with two polymer chains (crosslinking), allowing for the formulation of DDS with different nature, such as hydrogels or biopolymeric prodrugs. This tunability allows for tailored applications depending on the therapeutic needs. Dicarboxylic acid-terminated TKs were used to crosslink carboxymethyl chitosan (CMC), forming hydrogels (CMC-TK) with shear-thinning and self-healing properties—ideal for injectable or topical applications. These hydrogels exhibited selective degradation in pathological ROS concentrations (50–250 μM H_2O_2), reducing ROS to basal levels (0–5 μM) within 24 hours. They also demonstrated substantial antioxidant capacity, achieving a maximum radical scavenging activity of 88.9 ± 2.8% in 220 minutes, compared to 42.7 ± 5.8% in CMC controls. Additionally, no negative effect on the viability of PMA-differentiated THP1 macrophages was observed after interaction with CMC-TK, compared to CMC and other commercial crosslinkers. In parallel, diamino-terminated TKs were employed to functionalize hyaluronic acid and covalently attach the anti-inflammatory drug ketoprofen, forming a polymeric prodrug. Drug incorporation was confirmed via NMR, FTIR, and UV spectroscopy, with varying loading degrees depending on reaction conditions. These systems showed enhanced and selective drug release in oxidative environments, with significantly higher ketoprofen release in the presence of H_2O_2 compared to passive diffusion. In this work, we demonstrated that thioketals can be effectively combined with biopolymers to create smart ROS-responsive materials with tailored properties. Beyond offering the first insight into their innate antioxidant activity, these ROS-responsive materials could potentially increase the treatment efficiency and reduce side effects for antioxidant and/or anti-inflammatory therapies, acting only in those tissues affected by an oxidative environment. These materials may also be adapted for other bioactive payloads or biopolymers, broadening their future therapeutic potential.

(0030)

Decellularized kidney extracellular matrix: a tunable biopolymer for renal repair

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Decellularized kidney extracellular matrix (DKECM) is a bioactive polymer derived from porcine renal tissue via removal of cellular components while retaining native ECM proteins and growth factors that regulate cell behavior and tissue remodeling. Our first study developed a thermoresponsive DKECM hydrogel and explored its biocompatibility for renal regeneration. Upon interaction with macrophages, the hydrogel induced both M1 and M2 polarization, suggesting a balanced immunomodulatory environment supportive of in-vivo integration. Additionally, encapsulating renal progenitor cells (RPCs) within the DKECM hydrogel resulted in superior viability and proliferation compared to collagen I control, with sustained expression of tubular and podocyte markers over long-term culture. To further exploit DKECM's versatility, we formulated a kidney-specific bioink that preserves native biochemical cues and supports tunable porosity for the controlled release of RPC-derived extracellular vesicles (EVs). Bioprinting this bioink yielded a fish-net–shaped construct tailored for direct application onto lesioned kidney surfaces; it demonstrated structural integrity and sustained EV release for up to 14 days. In an in vitro model of ischemia-reperfusion injury using HK-2 tubular epithelial cells, EVs promoted a balanced regenerative response: under hypoxia, Ki67 staining indicated an increase in proliferative cells, which normalized toward baseline upon EV treatment, suggesting that EVs can modulate the excessive proliferation induced by hypoxia; reactive oxygen species levels were lower in EV-treated cultures versus untreated hypoxic controls, demonstrating the protective effect of EVs against oxidative stress; and EV administration reduced SOX9 expression by 40 % relative to hypoxia alone, reflecting modulation of injury-induced repair pathways. Ongoing work explores DKECM in micronized powder form as a self-assembling core within co-culture spheroids of RPCs and HUVECs. During aggregation, powdered DKECM localizes centrally, enhancing the expression of differentiation markers and upregulating renal genes compared to matrix-free spheroids. Aquaporin-1 and Wilms tumor 1 are key markers of tubular cells and podocytes, respectively, and are upregulated in conditions with higher DKECM concentration. Migration and fusion assays further reveal accelerated fusion kinetics in matrix-containing constructs, consistent with advanced cellular maturation. Collectively, these studies underscore DKECM's potential as a multifunctional biomedical polymer for kidney regeneration, spanning injectable hydrogels, organ-specific bio-inks, and biofunctional powders. By combining tissue-specific biochemical signals with tunable mechanical and release properties, DKECM-based materials offer a powerful, cell-free platform for precise, organ-targeted regenerative therapies.

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(0031)

Microfluidic manipulation of biomedical polymers for the biofabrication of miniaturized 3D cancer architectures

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The functionality of living tissues, healthy or diseased, is connected to their complex 3D shapes. Approaching such characteristics by finely tuning cell/material organization is crucial for engineering in vitro tissues for biomedical testing. High-throughput and efficient data extraction are additional requisites for enhancing the potential of these engineered tissues for widespread in vitro testing. In this work, we leverage microfluidic flows to organize hydrogel precursors (biopolymers) and fabricate diverse biological architectures within multi-material, multi-cellular hydrogel microfibers that emulate functional 3D cell arrangements, particularly focusing on cancer. Computational modeling is employed to predict cell/material organization, while high-throughput microscopy and other optical-driven tools facilitate the efficient digitalization of biological events. A natural biomedical polymer toolbox comprising Gellan Gum, Alginate, GelMA, GelTrex, Collagen, and others was employed to fabricate hydrogel microarchitectures with varying shapes and compositions. Precursor viscosity and flow characteristics were modeled and optimized to modify the 3D arrangement of compartments within hydrogel fibers of multiple configurations. Wet-spinning with Calcium Chloride was then utilized to crosslink the hydrogel precursors into distinct micro-fiber architectures which can approach the intricate 3D architectures of all different types of cancer configurations, such as layered architectures, solid fiberoids, glandular structures, or size-controlled spheroids. Diverse hydrogel fiber architectures were successfully produced by manipulating hydrogel precursor viscosity and channel organization within one similar wet-spinning approach. Ribbon-like shapes were utilized to integrate two cellular compartments (cancer and stroma), separated by a thin basement membrane, thus recapitulating the early stages of pre-metastatic layered-like cancer cell invasion, in vitro. Core-shell shapes were further fine-tuned to cultivate living cancer fiberoids (fiber-shaped organoids) in continuous fibers approaching solid cancer structures. Alternatively, a similar architecture was employed in reverse organization to approach the cellular layer surrounding an acellular lumen present in glandular tumors such as those of breast and prostate. Finally, a multi-phase approach also enabled the sequential generation of hydrogel-lined medium pockets for the controlled growth of spheroids. The different cancer configurations were put to test with varied therapeutic strategies depending on the types of cancer under culture, to prove the efficiency of these soft 3D architectures in drug discovery and optimization. The flow-driven assembly of hydrogel/cell fiber constructs proved to be an extremely versatile technology, highly adaptable for the high-throughput fabrication of living 3D cancer architectures in varied configurations. Moreover, these small architectures facilitate the direct quantification of biological events and therapies' outcomes with high throughput.

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(0032)

Electroactive nanocomposite hydrogels for bone repair: integration of nanohydroxyapatite-decorated carbon nanotubes

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Advances in bone tissue engineering emphasize functional biomaterials to overcome graft limitations. Hydrogels present minimally invasive alternative for delivering bioactive cues and cells to promote bone regeneration. Incorporating nanomaterials enhances their mechanical, biological, and therapeutic potential. This study developed an injectable nanocomposite hydrogel with improved mechanical strength and osteoinductive properties. Methacrylated gellan gum (GGMA) was synthesized via glycidyl methacrylate modification. Carbon nanotubes (CNTs) were coated with nano-hydroxyapatite (nHAp) through Ca^{2}-mediated nucleation and phosphate addition to mimic hydroxyapatite self-assembly on collagen fibrils. Three hydrogel formulations—GGMA, GGMA–CNT, and GGMA–nHApCNT—were evaluated. Cationic gelation formed hydrogels, which were analyzed for rheology, structure, bioactivity, antioxidant and antibacterial properties, angiogenic potential, conductivity, and hemocompatibility. Human adipose-derived stem cells were encapsulated and cultured under basal and osteogenic conditions. Assessments included viability, proliferation, metabolic activity, alkaline phosphatase, and gene expression. NMR and spectroscopy confirmed GGMA methacrylation and nHAp formation on CNTs. nHAp functionalization enhanced hydrogel's mechanical properties. Micro-CT revealed that GGMA–nHApCNT presented 0.117 µm wall thickness, 0.042 µm pore size, and 9.08% porosity. Injectability tests showed CNTs increased injection force (6.6 N), whereas nHApCNT reduced it (5.6 N vs. 6.1 N for GGMA), indicating improved injectability. Bioactivity assays showed enhanced mineralization in GGMA–nHApCNT. Both CNT-based hydrogels exhibited ~25% antibacterial activity, and while GGMA–nHApCNT retained antioxidant properties, a 30% decrease was observed. Conductivity tests confirmed all hydrogels were conductive, with GGMA–nHApCNT highest at 0.029 S/m. CAM assays demonstrated superior angiogenesis in GGMA–nHApCNT. Cell studies showed GGMA–nHApCNT promoted higher viability (20% > GGMA, 80% > GGMA–CNT), greater cell spreading, and stronger osteogenic gene expression. Hemocompatibility was favorable for GGMA and GGMA–nHApCNT, with <1% hemolysis, unlike GGMA–CNT (5%). Altogether, GGMA–nHApCNT hydrogels combine improved stability, bioactivity, conductivity, and cell response. The reduced injection force supports minimally invasive delivery, and the multifunctional properties suggest strong potential for bone regeneration. This nanocomposite hydrogel platform addresses current scaffold limitations and informs the design of next-generation biomaterials in regenerative medicine.

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(0033)

A biomimetic microfluidic strategy for efficient tumor cell isolation using electrospun membranes

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Metastasis, the leading cause of cancer-related mortality, is driven by the spread of tumor cells through the bloodstream [1]. Circulating tumor cells (CTCs), shed from primary or metastatic sites, offer a minimally invasive means to monitor cancer progression and treatment response. However, isolating viable CTCs remains difficult due to their rarity—just a few among millions of blood cells per milliliter—and biological heterogeneity [2,3]. Recent advances in micro- and nano-technologies, especially microfluidic systems, have shown promise for sensitive, specific, and viable CTC capture and downstream analysis [4]. In this context, we present a multilayer microfluidic device integrating a removable electrospun polycaprolactone (PCL) membrane designed to enhance tumor cell capture and post-isolation culture. The ONCO-CTC chip, fabricated from bonded PDMS layers, features a central chamber housing the membrane, which was manufactured using controlled electrospinning parameters [5]. Scanning electron microscopy (SEM) and micro-computed tomography (microCT) confirmed a porous, highly interconnected membrane structure (porosity: 13.1±0.9%; interconnectivity: 88.5 ± 1.1%) optimized for cell retention and nutrient exchange. When challenged with HCT-116 colorectal cancer cells, the system achieved a cell capture efficiency of 94±2.6%—significantly higher than the commercial ScreenCell® system, which reached only 82±10.9%. Retained cells were identified via EpCAM-FITC and DAPI staining. After 72 hours of culture on retrieved membranes, cells showed significantly higher viability as compared to those cultured on commercial membranes (613.4 ± 126 vs. 15.4 ± 0.5; $p < 0.01$), as measured by PrestoBlue® assay and observed by Calcein-AM/PI staining. This bioengineered platform enables modular, biologically compatible tumor cell capture and culture, overcoming the limitations of traditional rigid filters. Its gentle flow dynamics and ease of membrane retrieval support downstream analyses for various diagnostic or research applications. The reproducibility and adaptability of the ONCO-CTC highlight its strong potential as a next-generation tool in liquid biopsy for cancer diagnostics and personalized treatment planning.

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(0034)

Incorporation of acidic monomers into responsive nanogels modulates antimicrobial release and enhances penetration into bovine udder tissue

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Bovine mastitis (BM) is an inflammation mainly produced by bacterial colonization of mammary tissue.[1] On dairy farms, antibiotics remain the primary method for managing BM. However, the widespread use of antibiotics in animals has accelerated the development of antimicrobial resistance (AMR), leading to a serious threat to both animal welfare and human health.[2] In response to this growing concern, multi-responsive nanogels (NGs) were engineered to deliver nisin, an antimicrobial peptide, specifically under infection-related conditions, thereby avoiding unnecessary exposure to antimicrobials. Infection environment typically exhibits an increase of the local temperature while a reduction in pH levels.[3] Thus, the designed NGs were intended to release nisin in response to these environmental triggers. To achieve this, a library of NGs was synthesized by copolymerizing N-isopropyl acrylamide (NIPAM) with the acidic monomers methacrylic acid (MAA) and acrylic acid (AA), using partially acrylated dendritic polyglycerol as a crosslinker. The incorporation of AA and MAA enabled the NGs to undergo a temperature-sensitive transition triggered by acidic conditions typical of infection. The pH-dependent thermal behavior of the NGs was characterized using transmittance measurements, dynamic light scattering (DLS), and small-angle X-ray scattering (SAXS). These analyses, supported by theoretical calculations, confirmed that NGs containing 5% AA and 10% MAA exhibited a clear pH-triggered thermal transition. To evaluate the pH-thermal response, nisin was encapsulated inside NGs with 5% AA and 10% MAA, but we observed that the peptide was mainly released by diffusion rather than through stimulus-triggered release. To address this issue, bovine serum albumin (BSA) was incorporated into the formulation. Nisin was first complexed with BSA and then encapsulated inside the NGs, achieving release triggered by the infection-related decrease in pH and increase in temperature. The sample containing 5% AA showed the best performance, releasing nisin effectively under infection conditions while retaining a high amount of the cargo under healthy udder conditions. The penetration of NGs with different AA and MAA percentages was evaluated using an ex vivo bovine udder model. We observed that the incorporation of acidic monomers enhanced NG penetration into udder tissue. Additionally, all NG formulations demonstrated no toxicity toward bovine cells in vitro. Together, our results highlight the potential of multi-responsive NGs to improve drug delivery to udder tissue, optimize antimicrobial use, extend retention time, and help prevent the development of AMR.

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(0035)

Biomimetic blood-brain barrier model engineered via cell sheet technology and microfluidics

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The blood-brain barrier (BBB) is a selectively permeable interface essential for preserving brain homeostasis. Besides its physiological functions, BBB presents a major obstacle to drug delivery targeting central nervous system (CNS) disorders such as Alzheimer's disease and brain tumors. Thus, there is growing interest in establishing high-fidelity *in vitro* BBB models for drug screening and development. In this study, we developed a biomimetic BBB model by integrating cell sheet engineering with a microfluidic dynamic culture system. The model was built from human brain microvascular endothelial cells, human brain vascular pericytes, and human astrocytes grown in a layered fashion to enable cell-cell communication. We optimized the seeding, culture, and maintenance conditions to obtain an *in vitro* platform that comprises essential elements of the BBB such as multicellularity, cellular order, three-dimensionality, and differentiated basement membrane. Our results showed that cell sheet technology enabled the co-culture of endothelial cells, pericytes, and astrocytes, replicating the native BBB architecture, enhancing cell–cell interactions, and eliminating the need for synthetic membranes by promoting endogenous extracellular matrix production. Moreover, we demonstrate that the engineered BBB is handleable and convenient to use in different setups - we assessed the model performance under static and dynamic conditions. The exposure of the BBB model to flow in a microfluidic device provided physiological stimulation via shear stress. This stimulation resulted in adjustment of cell morphology and expression of cell-specific genes and proteins needed for the BBB function. The induced changes ultimately lead to formation of tight junctions and more selective permeability in comparison to the static model. Finally, the use of the engineered BBB model in the glioblastoma scenario was also demonstrated and validated using established chemotherapeutic. Altogether, our results showed that the proposed innovative BBB model offers a robust and dynamic platform for CNS drug testing, advancing the development of more effective therapies for neurological diseases.

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(0036)
Adhesive and hemostatic microneedles based on biomaterials

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Uncontrolled bleeding resulting from trauma, disease, or surgery remains a critical clinical challenge, often leading to hypothermia, hemorrhagic shock, or organ failure. Rapid hemostasis is essential to prevent these outcomes. While traditional methods such as sutures and staples mechanically seal wounds, they frequently cause scarring and require professional intervention. Although biomaterial-based hemostats offer biocompatibility, they typically lack strong adhesion and are insufficient for severe bleeding. To address these limitations, we developed an adhesive hemostatic microneedle (MN) patch capable of rapid blood absorption, coagulation, and wound sealing with minimal invasiveness. The patch was fabricated using a biocompatible gelatin methacryloyl (GelMA) base and incorporated cuttlefish bone powder for enhanced coagulation and polydopamine (PDA) for improved tissue adhesion. Polydimethylsiloxane (PDMS) molds and vacuum-assisted casting enabled precise MN formation. Mechanical evaluations, including burst pressure and adhesion tests, confirmed the patch's stability under bleeding conditions. Both in vitro and in vivo studies demonstrated the patch's effective hemostatic performance, highlighting its potential for emergency and surgical applications.

(0037)

Engineered injectable antibacterial spider silk-alginate hydrogels for veterinary wound healing

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Dental disorders are among the most frequently reported conditions in veterinary care facilities, with periodontal disease (PD) being particularly prevalent in both cats and dogs [1,2]. PD is a multifactorial inflammatory disease resulting from a complex interplay between subgingival plaque bacteria and the host's immune response [2]. Current therapies have several limitations, which diminishes treatment success and can lead to further complications that must be addressed. Spider silk, known for its exceptional biocompatibility, mechanical strength, and inherent antimicrobial properties, has emerged as a promising biomaterial for medical and veterinary applications, particularly in wound healing [3]. In this study, we explore the potential of antimicrobial spider silk-based hydrogel for veterinary wound healing using sodium alginate as the primary matrix component. To achieve this goal, we developed new hydrogels by combining bioengineered spider silk proteins fused with an antimicrobial protein (2%, 6mer-HNP1), bioengineered spider silk protein alone (2%, 6mer), and sodium alginate (3%, 6%, 12%, SA) crosslinked with calcium chloride (20 mM). Different spider silk protein-to-alginate ratios (1:1 to 1:4) were produced, and we assessed their rheological properties. We also further evaluated the cytotoxicity of the spider silk-alginate hydrogels. We successfully fabricated a new biomaterial with injectability potential. Rheological analysis revealed that all hydrogel formulations exhibited solid-like behavior. Regardless of the spider silk protein-to-alginate ratio, hydrogels with 6mer or 6mer-HNP1 and 3% SA exhibited rheological parameters closely aligned with those ideal for bioink applications. In contrast, hydrogels made with 6% or 12% SA resulted in stiffer materials, potentially compromising printability. Additionally, the presence of the spider silk protein may have hindered hydrogel formation at higher concentrations, thus contributing to reduced rheological properties. Furthermore, no cytotoxic effect was observed with the developed hydrogels. Overall, these findings provide new insights into using recombinant spider silk proteins with antimicrobial peptides to develop multifunctional hydrogel constructs as injectable wound healing materials, creating a favorable environment to hinder the progression of periodontal disease.

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(0038)

Bioactive magnesium-collagen/ha hydrogel crosslinked by visible light for infected wound healing

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Skin, as the outermost barrier of the body, is highly vulnerable to wounds and injuries. Without timely and proper treatment, these wounds are at risk of infection, emphasizing the importance of effective wound care. Bacterial infection is a key factor that delays the wound healing process; therefore, its suppression is crutial for promoting rapid tissue regeneration. However, conventional wound dressings generally lack inherent antibacterial properties, and traditional antimicrobial agents, such as inorganic compounds or antibiotics, may lead to systemic toxicity and contribute to antibiotic resistance. In this study, we developed a collagen-based hydrogel crosslinked by visible light, into which magnesium ions (Mg^{2+}) were incorporated to confer antibacterial functionality as a wound dressing. The Mg^{2+}-loaded hydrogel exhibited excellent biocompatibility, strong tissue adhesion, and notable antibacterial efficacy, achieving approximately 70% inhibition against *Staphylococcus aureus* Furthermore, in a full-thickness skin defect mouse model, the Mg^{2+}-loaded composite hydrogel effectively suppressed bacterial growth and accelerated wound repair. This novel Mg^{2+}-loaded collagen–hyaluronic acid hydrogel platform offers a promising strategy for infected wound treatment by synergistically combining antibacterial properties, tissue adhesion, and enhanced regenerative capacity.

(0039)
Bioactive plcl nanofibers for enhanced wound healing

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Effective wound healing remains a significant clinical challenge, particularly in cases of chronic and hard-to-heal skin defects. Conventional treatment approaches often fail to adequately support the regenerative processes required for complete recovery. Therefore, the development of advanced biomaterials functionalized with bioactive products is essential to enhance tissue regeneration and accelerate wound healing. This study is aimed at synthesizing hybrid nanofibers from poly(L-lactide-co-ε-caprolactone) (PLCL) via electrospinning, incorporating bioactive molecules derived from young Wharton's jelly mesenchymal stem cells (WJ-MSCs) from umbilical cord. The bioactivity of nanofibers was subsequently evaluated *in vitro* on human adipose-derived MSCs (hASCs) isolated from adult donors. The bioactive nanofibers were obtained by electrospinning in different configurations (random and aligned) following a protocol developed by the Institute for Bioengineering of Catalonia (IBEC)[1]. The resulting nanofibers were characterized by light microscopy imaging and atomic force microscopy (AFM) to determine the fibers' diameter. Additionally, the release kinetics of the incorporated FITC-labeled bioactive molecules were analyzed. The biocompatibility of the nanofibers was evaluated using hASCs, assessing their adhesion, overall morphology, and directed migration through an *in vitro* wound healing assay. The data obtained in this study demonstrates that the bioactive molecules derived from MSCs were successfully incorporated into the PLCL nanofibers and were gradually released into the surrounding microenvironment, supporting cell viability and stimulating cell migration. The wound healing assay further revealed faster and more efficient wound closure when the cells were in contact with aligned nanofibers compared to randomly oriented ones. These findings suggest that the alignment of nanofibers provides both biochemical and structural cues, contributing to enhanced tissue regeneration. This study highlights the potential of the hybrid PLCL nanofibers as an effective carrier of the bioactive compounds for applications in the field of regenerative medicine. Future studies will focus on optimizing the release profile, conducting *in vivo* evaluations, and exploring the potential clinical application of the bioactive nanofibers for the treatment of chronic wounds.

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(0040)
Tuning macrophages responses with fibroblasts-derived extracellular matrix

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Introduction: 3D in vitro skin models offer a valuable platform to study molecular pathways otherwise restricted to animal models. However, their physiological relevance is limited by poor extracellular matrix (ECM) mimicry [1] and reduced cellular representation. To tackle these limitations, we established a protocol to extract fibroblasts-derived ECM and used it to prepare immunocompetent in vitro skin models. We hypothesize that combining ECM extracts with macrophages supports a more physiologically relevant immune microenvironment.
Methods: Core(cECM) and core-associated (caECM) ECM components were extracted from fibroblast cultures using an in-house protocol. Blood monocytes were differentiated into macrophages (MDMs) with M-CSF (50 ng/mL) and exposed to varying ECM concentrations (caECM:5, 25, 50 µg/mL;cECM: 250, 500, 1000, 2000µg/mL). The response to ECM was also assessed in the presence of TNFα (100ng/mL), to understand its influence on a pro-inflammatory environment. MDMs phenotypic shifts were assessed by RT-PCR (NF-kB,STAT1, PPARG,JMJD3), flow cytometry (CD68,CD86, CD319, CD206), and multiplex cytokine analysis (IL-6,CXCL10,TNF-α,CCL18,CCL22). The phagocytic capacity was evaluated by western blot (CD68,LAMP1,LAMP2), flow cytometry(SSC) and TEM.Antigen presentation capability was assessed in MDMs exposed to opsonized latex beads by flow cytometry (MHC II).
Results: Exposure to fibroblast-derived ECM did not induce a pro-inflammatory shift, as M1-like markers levels remained below those in control M1 MDMs, despite a dose-dependent increase in CD86/CD319 surface expression, and IL-6/CXCL10 secretion in response to cECM. In contrast, ECM stimulation, particularly with caECM, induced expression of the M2-associated marker CD206, and CCL18 and CCL22 secretion, promoting a shift toward a M2-like phenotype. Co-stimulation with cECM and TNF-α reduced IL-6, CXCL10, TNFα production while increasing CD68 expression in MDMs. Additionally, cECM enhanced the percentage of MDMs with higher granularity (SSC), promoted vesicle accumulation (TEM), and upregulated lysosomal markers (CD68, LAMP1). Approximately 50% of cECM-treated MDMs with elevated granularity also exhibited bead internalization and CD68 expression, but reduced MHC II levels.
Discussion and Conclusions: Fibroblasts-derived ECM does not promote a pro-inflammatory phenotype, even if obtained from different donors. cECM modulates pro-inflammatory responses while promoting MDMS phagocytic and lysosomal activity without enhancing MHC II-mediated antigen presentation. These findings suggest that fibroblasts-derived ECM supports a non-activated homeostatic macrophage phenotype, reinforcing its potential to improve the physiological relevance of immunocompetent 3D skin models.

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(0041)

Exploring the immunogenecity of gellan gum-based inks for 3D bioprinting of human macrophage-integrating human tissues

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Immunocompetent 3D tissue models are fundamental for investigating immune cell behavior in contexts including autoimmune diseases, allergies, cancer, wound healing, and therapy response. A major challenge lies in selecting biomaterials that support cells without unintentionally activating immune responses. Since gellan gum (GG), a low-immunogenic polymer, has shown promise in supporting key functions within 3D bioprinted constructs, herein we investigate how variations in GG concentration and the presence/absence of a cell-adhesive peptide (cyclicRGD) affect the phenotype and activation of human monocyte-derived macrophages (MDMs) under external stimulation. Monocytes isolated from peripheral blood mononuclear cells were differentiated into MDMs with M-CSF and encapsulated in GG-based ink formulations (with/without cyclicRGD; low/high polymer content). Cell viability (calcein/propidium iodide staining), adhesion (phalloidin staining), and phenotype (phosphorylation multi-pathway array/luminex) were assessed, and the activation of classical or alternative pathways was analyzed under different external stimulation (IFN-γ+LPS or IL-4) regimens. MDM viability was not compromised by the tested formulations, but cell morphology varied from a round shape in the absence of cyclicRGD to an adhesive-like stretched form in cyclicRGD-containing formulations. Within 24h in the absence of cyclicRGD, higher polymer content promoted ($p<0.05$) the phosphorylation of regulators of MAPK (MSK2/MMK6) and NFkB (ATM) while reducing ($p<0.05$) the phosphorylated forms of JAK/STAT (TYK2/EGFR), TGFb (ATF2), AKT (BAD/GSK3B/p27) and MAPK (MEK) signaling pathways. In the presence of cyclicRGD, regulators of MAPK (ERK), NFkB (eIF2a/ATM) and AKT (mTOR/P70S6K) were also increased ($p<0.05$) for higher polymer content. Both pro-inflammatory (IL-1ß/IL-6/IL-12p40/TNF-α) and anti-inflammatory (IL-1RA/IL-10/CCL22) cytokines were detected, with most cytokines declining after 3 days. As the impact of the biomaterial on MDM behavior appeared minimal, the response to external stimuli was subsequently evaluated. Cells responded with the release of pro-(classical) and anti-inflammatory (alternative) mediators ($p<0.05$), with levels varying according to polymer content in the absence of cyclicRGD ($p<0.001$). To assess long-term responsiveness, MDMs were subjected either to continuous stimulation (up to 10 days with media replenishment every 2–3 days) or to a secondary stimulus (48h) following a 5-day resting phase. In both cases, cells remained responsive, though continuous stimulation resulted in reduced IL-6 and TNF-α secretion, highlighting an influence of prolonged culture. Notably, CXCL10 secretion was the only cytokine affected by polymer content in the absence of cyclicRGD, indicating that long-term MDM functionality is not primarily determined by the biomaterial. Overall,these findings demonstrate that GG-based inks support MDM responsiveness without activation,enabling immunocompetent bioprinting 3D tissue models.

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(0042)

Multifunctional collagen and cellulose nanofiber mat containing peptide drug for hemostasis and skin repair

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Skin repair remains a critical challenge in modern medicine, as impaired healing can lead to chronic wounds, infections, and delayed tissue regeneration. In this study, we fabricated multifunctional collagen and cellulose nanofiber mat containing peptide drug to enhance skin repair and studied biological properties such as hemostasis and skin regeneration. The collagen and cellulose nanofiber mats containing peptide drug were fabricated using electrospinning. Fourier transform infrared spectroscopy was used to confirm collagen and cellulose in the nanofiber mat. The morphology and mechanical properties of the nanofiber mats were characterized using scanning electron microscopy and universal testing machine, respectively. The biocompatibility of the nanofiber mat was assessed by cell viability assay and hematoxylin and eosin staining. The multifunctional skin repair efficacy also was evaluated using hemostatic assay and in vivo wound closure analysis. The results of the biocompatibility assessments demonstrated that the collagen and cellulose nanofiber mat was nonirritating and suitable for skin repair applications. The hemostatic assay showed that the collagen and cellulose nanofiber mat exhibited a 5 fold increase in hemostatic function compared to the control, indicating its potential for rapid bleeding control. And in vivo wound healing experiments demonstrated that the collagen and cellulose nanofiber mat significantly accelerated wound remodeling compared to conventional gauze and cellulose nanofiber mat. These results indicate that the collagen and cellulose nanofiber mat possesses multifunctional properties that enhance skin repair by promoting hemostasis and accelerating skin regeneration.

(0043)

A self-healing alginate hydrogel enriched with ecm cues to promote vascularization and skeletal muscle regeneration

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Skeletal muscle (SKM) intrinsic regenerative potential is significantly compromised following severe injuries. Current clinical interventions, such as autologous muscle flaps, are constrained by donor site morbidity and inadequate vascularization, limiting tissue recovery [1]. Injectable cell-laden biomaterials offer a minimally invasive alternative, faster recovery, and reduced healthcare costs. Self-healing hydrogels are particularly promising due to their dynamic crosslinking, enabling post-injection integrity and sustainable delivery of bioactive cues [2]. However, the limited ability of hydrogel-based 3D constructs to support rapid neo-vascularization often leads to necrosis and, thus, graft failure. To address this challenge, we developed a self-healing alginate hydrogel enriched with extracellular matrix (ECM) cues to foster a SKM-specific, pro-angiogenic microenvironment. The self-healing hydrogel was formulated by synthesising hydrazide-modified (ALG-ADH) and oxidized (ALG-OXI) alginates, and subsequently combined with SKM-derived decellularized ECM (dECM). The successful synthesis of alginate derivatives was confirmed by ^{1}H-NMR and GPC. Moreover, rheological analysis revealed that the addition of ECM cues did not impair the hydrogel's self-healing capacity. Following three high-strain deformation cycles (G">>G'), the storage modulus (G') recovered to near-initial values, indicating robust mechanical self-recovery. Concerning biological performance, C2C12 myoblasts were embedded within the hydrogel and cultured for 7 days. Resazurin assay and confocal immunofluorescence imaging revealed an increased metabolic activity over culture time and characteristic elongated cell morphology, respectively, suggesting favourable myogenic compatibility. To evaluate the angiogenic potential, vascular units (VUs) composed of human umbilical cord-derived endothelial cells and fibroblasts [3] were embedded in the produced hydrogel. After 7 days, the self-healing hydrogels not only supported VU's cells' outward migration but also enabled the formation of capillary-like structures. While self-healing hydrogels with ECM cues have been explored in other tissue engineering applications, their use in SKM regeneration remains unexplored. Interestingly, here, we demonstrated that the enrichment of the self-healing alginate hydrogel with SKM-dECM not only preserved the hydrogel's self-healing properties but also enhanced its bioactivity, supporting both myoblast growth and the formation of vascular-like structures. These findings underscore the promise of this ECM-integrated, self-healing hydrogel for promoting vascularized skeletal muscle regeneration.

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(0044)

3D in vitro models of osteosarcoma: a novel hydrogel-scaffold system for therapeutic research

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Osteosarcoma (OS) is the most common malignant bone tumor affecting children, adolescents, and young adults. While standard treatments, including surgery and chemotherapy, have improved the 5-year survival rate to 66%, therapy resistance, recurrence, and adverse side effects remain major challenges. This underscores the need for innovative treatments. OS malignancy is strongly influenced by its complex tumor microenvironment, which includes a small population of Cancer Stem Cells (CSCs) with self-renewing and pluripotent capabilities. This study presents a novel 3D *in vitro* model using enriched CSCs embedded in a hydrogel matrix as core within a bone-mimicking scaffold, aiming to replicate the CSCs niche in OS. The hydrogel is composed of 1% gellan gum (GG) and 0.3% hyaluronic acid (HA)—a polysaccharide derived from bacteria and a major extracellular matrix component, respectively. GG was solubilized at 2% (w/v) in water at 70°C, while HA was prepared at 3% in water at room temperature. CSCs were enriched over 10 days induction by a well-established Sarcospheres-Forming Culture, and embedded in the hydrogel ($3.2x10^5$ cells/mL). Then, the hydrogel was extruded through a 18G needle, with gelation initiated by cation solutions like PBS or cell culture media within minutes. Preliminary evaluations of CSCs viability and morphology in the hydrogel up to 12 days (via PrestoBlue and live/dead assays) confirmed the cytocompatibility of the hydrogel system. Additionally, injecting the hydrogel into a bone-like scaffold demonstrated the feasibility of this model. These promising results suggest that this hydrogel-scaffold system could support the development of complex models for studying OS tumor behavior and for drug screening applications.

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(0045)

Injectable and degradable oxidized alginate hydrogels incorporating PANI:PSS nanoparticles for advanced photothermal therapy

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Photothermal therapy has emerged as a noteworthy alternative to traditional cancer therapies, including radiation therapy and chemotherapy. However, conventional photothermal agents are typically present as nanoparticles, which are too small to persist in the target tissue, resulting in their rapid elimination. Additionally, conventional photothermal agents tend to be either expensive or complex to produce. To address these challenges, we introduce hydrogels composed of oxidized alginate polymer network, incorporating polyaniline:poly(sodium 4-styrenesulfonate) (PANI:PSS) nanoparticles within the polymer matrix. These oxidized alginate PANI:PSS hydrogels showed excellent injectability as well as controllable degradation rates, which varied from several days to several months, according to the oxidation degree of alginate chains. Furthermore, these hydrogels exhibit a remarkable photothermal effect, even in a neutral pH environment. Upon near-infrared (NIR) irradiation, the temperature of the hydrogel rapidly increased to 53 °C within 5 min, implying its strong applicability as an advanced photothermal agent for photothermal therapy.

(0046)

Investigating bioengineered spider silk sutures - from antibacterial properties to immune dynamics

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Sutures are among the most established surgical devices, primarily valued for their mechanical role in wound closure. Despite their widespread use in medicine, surgical site infections remain a major cause of delayed healing and postoperative complications, highlighting the need for more advanced suture technologies. Spider silk is an attractive material due to its tunable mechanical strength, biocompatibility, and functional versatility (1-2). Moreover, recombinant DNA technology allows bioengineering spider silk proteins with antimicrobial peptides (AMP). In our previous work, we demonstrated that using antimicrobial peptide (AMP)-functionalized spider silk (6mer-HNP1) as an antibacterial drug-free coating for commercial silk sutures (Perma-Hand), significantly reduced Staphylococcus aureus and Escherichia coli colonization without compromising suture mechanics or cytocompatibility (1-2) at wound interfaces. Building on this, our current research shifts focus on immune modulation, aiming to understand how AMP-silk materials influence host immune responses, particularly macrophage behavior. Macrophages are crucial regulators of inflammation and tissue repair, capable of exhibiting various functional phenotypes depending on their microenvironment. We have established expertise in using precision technologies to reprogram macrophage responses (3-5), which provides valuable insights for investigating how AMP-functionalized silk may modulate macrophage functional states in the context of infection and healing. By reducing bacterial burden, AMP-silk materials not only mitigate inflammatory triggers but also engage with immune cells in ways that remain poorly understood. This dual mechanism may help prevent unresolved inflammation, biofilm-related immune activation, and fibrotic encapsulation. In this study, we explore how AMP-functionalized silk affects macrophage phenotypes, cytokine signaling, and immune cell recruitment under both sterile and bacteria-exposed conditions. Our goal is to determine how AMP-functionalized materials can shift macrophage responses toward regenerative, rather than pro-inflammatory, states—thereby reducing the risk of chronic inflammation and biofilm-related complications. This research offers a novel perspective on AMP-silk materials, advancing biologically-informed wound management. By exploring the immunomodulatory actions of AMP-functionalized silk, we take a critical step toward developing next-generation sutures that not only inhibit infection but can also actively engage with the immune system to promote optimal healing.

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(0047)

Preparation and evaluation of a novel dual-crosslinkable hybrid thermogel for tissue engineering

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Thermogels for biomedical applications that can be delivered and fill irregular spaces through minimally invasive technology have recently received great attention. However, conventional thermogels often suffer from poor mechanical strength and insufficient cell adhesion. To overcome this, we introduce a novel biohybrid thermogel with adjustable mechanical strength and improved cell adhesion. We synthesized a photo-crosslinkable thermogel, methacryl glycol chitosan (MGC), by *N*-methacrylation of glycol chitosan. To improve the cell adhesion properties of thermogel, a novel dual-crosslinkable MGC/GM scaffold system was developed by hybridizing biocompatible and photo-crosslinkable gelatin methacryloyl (GM). Our MGC/GM thermogel scaffold undergoes gelation at body temperature and exhibits enhanced mechanical properties through additional UV crosslinking even at low doses. Combining UV crosslinking and thermal gelation, our dual-crosslinking system provides versatility and tissue-customized property control. We compared the physicochemical and rheological properties according to the hybrid composition and analyzed their mechanical properties according to the various UV irradiation times. In addition, improved cell adhesion ability and high biocompatibility were confirmed. Therefore, MGC/GM hybrid thermogels demonstrate their potential as an effective injectable scaffold with customized properties for tissue engineering applications.

(0048)

Decellularized tendon-based injectable regenerative hydrogels: optimization of decellularization protocols and cross-species comparative analyses

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Tendons are uniaxial and flexible tissue bands connecting muscles to bones. Structurally, they have a hierarchically organized rope-like fiber arrangement and an extracellular matrix (ECM) rich in bioactive components. Its bioactive components play critical roles in regulating the regenerative and mechanical properties of tendon tissues. Oxidative stress, tendinopathies and acute ruptures that cause disruption of natural tendon ECM structure are the most common orthopedic injuries. For this purpose, biomaterials-based approaches including biological (allo-, xeno-, decellularized), synthetic or natural polymers are used. However, implanted approaches have significant limitations such as tissue collection, secondary damage due to open surgery and re-rupture. Next-generation approaches focus on the development of injectable hydrogels that can mimic ECM composition or enable delivery of therapeutics. However, most of the hydrogels have unsolved problems such as lack of tendon-ECM composition, low mechanical properties etc. Alternatively, the ECM can be substantially isolated using decellularization technology, allowing the use of natural tissues as injectable hydrogel. Until now, tendons isolated from various species such as bovine, human etc. have been decellularized and used in biomaterial development studies. But there are a limited number of studies based on injectable decellularized tendons for partial tendon injuries. Current studies focus on determining the optimal tendon sources and regulating the mechanical properties of ECM-derived hydrogels for further use. This study focuses on the development of decellularized tendon-based hydrogels for potential use in tendon repair and in-vitro tissue modeling studies. At the first stage, decellularization efficiency and bioactive contents of human and bovine Achilles tendon tissues were examined by comparative comprehensive analysis (DNA, H&E, collagen, growth factors, etc.). In this way, tendon tissue-based ECM with highly preserved bioactive content can be obtained by interspecies comparisons and optimal species for advanced applications were determined. In the second stage, optimization studies were carried out for an injectable tendon-tissue derived hydrogel system with high thermal sensitivity without the need for a secondary crosslinking agent. The findings showed that Achilles tendon tissues from both species could be decellularized with a common decellularization protocol optimized within the scope of the study. Although both tendon tissues have been found to retain a high bioactive content, taking regulatory considerations into account, it seems attractive to sustain the further click chemistry-based injectable hydrogel system with human-derived tissues.

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(0049)

Development and characterization of decellularized bone tissue-based bioadhesive regenerative hydrogel

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Bone tissue is a hard organ of the skeletal system that has numerous critical functions in the body. Bone tissue can self-regenerate after damage of a small size/diameter. However, it cannot repair itself after critical-sized damages such as extensive fractures and tumor resection. In these cases, surgical treatments involving the use of biomaterials become inevitable. Today, biological (allo-, auto-, xeno-grafts), synthetic, and natural biomaterials can be used for bone repair. Each of the biomaterials currently used in clinical settings still has unmet limitations. For instance, although biological grafts are considered the gold standard, they have disadvantages such as collection difficulty, limited source availability, and the risk of disease transmission. Similarly, while synthetic and natural polymers have advantages like mimicking the bone microenvironment and easy processability, they have drawbacks such as low mechanical strength and poor osteoconductive/inductive properties. It is important that the regenerative biomaterial has appropriate optimal surface topography, mechanical compatibility, bioadhesive, water retention and biodegradation behaviors specific to the target tissue. Biomaterials with various bioadhesive properties have been developed with the mentioned polymers with different production techniques. Similarly, implant surface coating materials are being developed to overcome the limitations of metal implants. On the other hand, a regenerative bioadhesive coating material that can fully mimic the target bone tissue microenvironment and provide effective adhesion at implant-surface-tissue interfaces has not been developed. In light of these known and unknown aspects, the aim of this study was to develop ECM-based bioadhesive hydrogels as regenerative biomaterials and implant coating materials. In the first part of the study, bovine cancellous bone tissues were decellularized by optimized decellularization protocols. Decellularization efficiency was determined (DNA, SEM, H&E etc.) followed by detailed bioactive content analysis (sGAG, collagen etc.). The findings showed that bovine cancellous bones can be decellularized with significant preservation of their bioactive content. In the second phase of the study, bone-based hydrogels were prepared and then the bioadhesive regenerative hydrogel was developed and characterized through chemical modification of ECM with dopamine. The efficiency of the modification was demonstrated by spectroscopic methods and the developed regenerative hydrogels were found to have optimal biocompatibility and bioadhesive properties. Our next goal is to evaluate the potential use of the developed regenerative bioadhesive hydrogel in coating functional metal implant surfaces.

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(0050)

Dopamine-functionalized hyaluronic acid hydrogels for anti-inflammatory delivery in neural tissue applications

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Introduction: Spinal cord injury (SCI) is a damage of the central nervous system that leads to severe, often permanent disabilities due to the disruption of neural connectivity. A challenge in SCI treatment is the lack of a supportive extracellular matrix (ECM) to guide axonal regeneration across the lesion site. Hyaluronic acid (HA) is a natural ECM component that plays a key role in neurogenesis and inflammation modulation, making it a good candidate for biomaterial targeting neural repair. However, native HA hydrogels possess poor mechanical strength and limited tissue adhesion, particularly in wet physiological environments. To address these limitations, we developed bioadhesive hydrogels based on dopamine-modified HA (HA-Cat), inspired by mussel adhesive proteins. Methods: HA with two different molecular weights (MW) was functionalized with adipic acid dihydrazide (HA-ADH) and with dopamine (HA-Cat). To introduce aldehyde groups, both native HA and HA-Cat were oxidized with sodium periodate, producing HA-A and HA-Cat-A, respectively. Then, hydrogels were formed by linking HA-ADH with either HA-A or HA-Cat-A via hydrazone bonds. Four different hydrogels were produced (HA_{613}, HA_{613}-Cat, HA_{828}, and HA_{828}-Cat), where 613 and 828 correspond to the sum of the MW of both HA derivatives. The hydrogels were subsequently freeze-dried and rehydrated in DMEM-F12. Ibuprofen (50 µM) was incorporated into HA-Cat-A prior to gelation. Results: HA_{613} and HA_{613}-Cat hydrogels were more stable after 7 days in DMEM/F12 culture medium and showed a higher stiffness (E'=16-20 kPa) than HA_{828} and HA_{828}-Cat, with values closer to *ex vivo* spinal cord. Moreover, HA_{613}-Cat hydrogels exhibited superior adhesive properties (731 ± 77 Pa, $\rho>0.001$) compared to the other hydrogels. To assess the biological performance, SH-SY5Y cells were cultured on the hydrogels. HA_{613}-Cat hydrogels supported high cell viability and attachment, while promoting favourable neuronal morphology. Furthermore, ibuprofen-loaded HA613-Cat hydrogels did not hinder cell growth. Conclusions: This work highlights the potential of HA-Cat hydrogels for clinical translation in neural tissue engineering and provides a platform for the localized delivery of therapeutic agents in SCI treatments.

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(0051)

Impact of the addition of beta tricalcium phosphate (ß-TCP) on the micro/nanotopography and cytocompatibility of poly(lactic-co-glycolic acid - PLGA) scaffolds for application in bone regenerative medicine

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Topographical characteristics of a biomaterial influence cell/substrate integration, a critical parameter for the development of scaffolds in bone regenerative medicine (BRM). However, the influence of parameters such as roughness, volume and surface index on cytocompatibility has not yet been widely explored. The aim of this research was to determine the topographical parameters of poly(lactic-co-glycolic acid - PLGA) scaffolds in their pure form and in composite with beta tricalcium phosphate (ß-TCP) and to characterize their influence on the cytocompatibility of osteogenic cells. PLGA and PLGA/ß-TCP scaffolds were manufactured by additive manufacturing using fused deposition modeling. The topographic characterization, on a micrometric scale, was carried out by profilometry using the following parameters: arithmetic average roughness (Sa), quadratic average (Sq), maximum roughness (Sz), surface index (SI), normal volume (Vn), Skewness (Ssk) and Kurtosis (Sku). Atomic force microscopy was used for the nanometric scale, using the parameters arithmetic mean roughness (Ra), quadratic mean roughness (Rq) and maximum roughness (Rmax). Cytocompatibility was established using the colorimetric viability test at 24 and 48 hours using the MG-63 osteogenic strain. The ANOVA method was used for statistical analysis, with a 5% significance level. The topographical results showed an increase in all the parameters in the PLGA/ß-TCP scaffold (Sa=75.6, Sq=87.1µm, Sz=405.9µm, SI=19.7µm, Vn=88.9µm, Ssk=-0.2µm and Sku=1.9µm; Ra=6.2nm, Rq=8.8nm and Rmax=126nm) compared to PLGA (Sa=20.4µm, Sq=27.1µm, Sz=189.3µm, SI=9.4µm, Vn=57.1µm, Ssk=1.1µm and Sku=4.7µm; Ra=3.2nm, Rq=4.3nm and Rmax=63nm). The viability rate at 24 hours, which infers cell adhesion, was 17% higher in the PLGA/ß-TCP sample ($p<0.000$). On the other hand, the 48-hour analysis showed no difference in the expansion rate between the scaffolds. The topographical changes inherent in printed PLGA/ß-TCP scaffolds increased the rate of cell adhesion, a determining event in the process of integrating bone substitutes. The reproduction of these parameters will allow the manufacture of more cytocompatible scaffolds for application in MRO.

(0052)

Development of decellularized urinary bladder matrix based cryogel for promoting angiogenesis

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Decellularized extracellular matrix(dECM)-based scaffolds have demonstrated potential in promoting cellular migration and tissue regeneration. Vascular regeneration is crucial as the vascular system provides nutrients and oxygen to the engineered tissue. Even though a few tissues are supplied with nutrients and oxygen through diffusion, engineered tissue with distant capillaries over 200nm faces difficulties. Vascular endothelial growth factor (VEGF) plays a critical role in angiogenesis by stimulating cell proliferation and migration, but its therapeutic delivery remains challenging due to the need for precise dosing to avoid adverse effects. In this study, we developed dECM-based cryogel scaffolds with sustained vascular endothelial growth factor (VEGF) release properties to enhance angiogenesis in ischemic tissues. Tissue-derived dECM contains structural elements such as collagen, glycosaminoglycans, and growth factors that can improve cell growth, proliferation, and attachment, and have an advantage in minimal immunogenicity. The neovascularization potential of a VEGF-loaded dECM/heparin cryogel was studied in a mouse hindlimb ischemia model. Blood perfusion was tracked until day 28, and the corresponding laser Doppler perfusion index (LDPI) was improved by 80%. This platform is easily fabricated and has a sustained release, and has the potential to be used not only for neovascularization but also in various tissue engineering fields with different growth factors.

(0053)

Self-assembling ghk-based peptides: enhanced proteolytic stability for accelerated wound repair

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The tripeptide Glycyl-Histidine-Lysine (GHK) is known for its ability to induce skin remodelling and promote wound healing.[1] Its bioactivity is significantly enhanced upon complexation with copper ions (GHK-Cu) boosting the synthesis of collagen, elastin and proangiogenic factors, suppressing the inflammation, and promoting cell proliferation during the wound healing process.[2] However, GHK-Cu is unstable in the physiological environment due to its rapid proteolytic degradation, which hinders its effective use as a therapeutic agent.[3] Herein, we used nanoprotein engineering to enhance the stability and bioactivity of GHK through its conjugation with the peptide F_4D that contains four aromatic phenylalanines (F) and induces self-assembly via pi-pi stacking. We synthesised three peptide systems, namely: Pep1, GHK co-assembled with F_4D; Pep2, GHK covalently bonded to F_4D at the glycine residue (F_4D-GHK); and Pep3, GHK, covalently bonded to F_4D at the lysine residue (F_4D-KHG). These peptide systems generated supramolecular assemblies upon pH switch from basic to neutral. CD spectroscopy revealed ß-sheet-like organization of the self-assemblies and AFM showed formation of nanofibers/nanotapes with widths in the range 60 - 235 nm. ^{1}H NMR spectroscopy confirmed the Cu^{2+} binding to the GHK sequence of the tested systems. Proteinase K degradation assay was used to assess the stability of the peptides in the presence and absence of Cu^{2+}. The results showed that 60% of Pep3-Cu resisted proteolysis after 24h, while GHK alone was completely degraded after 30 min in contact with Proteinase K. A scratch wound-healing migration assay demonstrated that all peptides promoted HaCaT cells' migration but Pep3-Cu was the most effective: it induced 70% of wound closure after 24h. Moreover, Pep3-Cu upregulated the expression of proinflammatory cytokines IL-6 and IL-8, as well as MMP-9 that is involved in ECM remodelling and cell migration. Furthermore, Pep3-Cu enhanced the expression of VEGF, essential for the vascularization and re-epithelialization of the skin.[4] Finally, we also demonstrated that Pep3-Cu forms a biocompatible hydrogel, highlighting its potential as a patch for wound healing. In a summary, we successfully applied nanoprotein engineering to enhance GHK biostability and bioactivity in the wound healing context.

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(0054)

Enhanced tissue regeneration potential of the combinatorial treatment of photobiomodulation and nanofiber mat in skin wound healing

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Photobiomodulation (PBM), a non-invasive technique involving the application of biocompatible, tissue-penetrating light to modulate intracellular chromophores, has emerged as a promising approach for enhancing skin wound healing. However, its synergistic use with tissue-regenerative materials has shown even greater potential in promoting tissue repair. In this study, we developed a series of electrospun nanofiber mats composed of poly(D-lactide) (PDLA) and varying concentrations of activated carbon nanofiber nanoparticles (ACNF NPs). The concentrations of both the polymer solution and nanoparticles were optimized to achieve the desired mat characteristics, including thickness, light transparency, surface morphology, and cell proliferation potential. Cell viability assays such as CCK revealed that mats containing a lower concentration of ACNF NPs (25 μg/mL) significantly outperformed their higher-concentration counterparts in promoting cell proliferation. The optimized formulation, referred to as P2a, was further evaluated in combination with PBM in a skin wound healing model. The combinatorial treatment demonstrated markedly enhanced tissue regeneration compared to either PBM or P2a treatment alone. These findings highlight the potential of integrating PBM with engineered nanofiber mats as a highly effective strategy for skin wound healing, offering promising implications for future clinical applications.

(0055)

Human placental ecm hydrogels: a bioactive scaffold for regenerative medicine

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Decellularized extracellular matrix (ECM) bioscaffolds are gradually recognized for their regenerative potential in tissue engineering. Human placental tissue, an abundant and ethically acceptable source derived from childbirth, is a promising candidate due to its structural and biochemical similarity to fetal tissues. This study aims to develop and characterize injectable hydrogels, which are derived from decellularized placental ECM (PECM), offering an innovative biomaterial for regenerative applications. Placental tissues were subjected to enhanced perfusion-based decellularization using enzymatic and detergent treatments over 72 hours. The resulting acellular ECM was cryo-milled and lyophilized into a powdered form. Hydrogels were fabricated at three concentrations (10PECM, 15PECM, and 20PECM corresponding to 10, 15, and 20 mg/mL of PECM) via pepsin digestion in acidic conditions, followed by neutralization and thermal gelation at 37 °C. These were evaluated alongside standard collagen hydrogels for their structural, mechanical, and biological properties. A 72-hour decellularization period reduced residual cellular and nucleic acid content while preserving key ECM components such as collagen and glycosaminoglycans. Neutralization of pregel solution enabled successful gelation, with higher concentration formulations (15PECM and 20PECM) demonstrating improved mechanical strength and resistance to degradation. Although collagen hydrogels exhibited greater mechanical stiffness, PECM hydrogels showed excellent biocompatibility with endothelial and fibroblast cells, as confirmed by live/dead staining and MTS assays. Proteomic profiling of PECM hydrogels revealed the presence of regeneration-associated proteins, including Serpin E1 and IGFBP1, which are known to influence angiogenesis and tissue repair. *In vivo*, 15PECM hydrogels promoted favorable wound healing responses in a murine skin wound model. This study establishes a reproducible method for creating bioactive hydrogels from human placental ECM and highlights the critical influence of ECM concentration on hydrogel performance. PECM hydrogels represent a promising scaffold for regenerative medicine; still, further optimization of mechanical properties, sterilization techniques, and controlled degradation are crucial for clinical translation.

(0056)

Modulating Hydrogel Properties through Silk Fibroin Hydrolysis: A Strategy for Tissue Engineering Scaffolds

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Silk fibroin (SF), a natural protein polymer derived from *Bombyx mori* cocoons, has garnered increasing attention in the field of tissue engineering due to its excellent biocompatibility, biodegradability, and mechanical adaptability. However, its inherent properties such as slow gelation and brittleness when used alone often limit its standalone application in hydrogel-based scaffolds. To address these limitations and achieve controllable physical properties, we investigated the fabrication of SF/gellan gum (GG) composite hydrogels through controlled hydrolysis of SF, enabling precise modulation of its molecular weight.
In this study, SF was hydrolyzed under specific conditions to produce hydrolyzed silk fibroin (HSF) with reduced molecular weights. The HSF was subsequently blended with low-acyl gellan gum, a naturally derived anionic polysaccharide, and crosslinked via ion-induced physical gelation using calcium ions. The degree of SF hydrolysis was systematically varied to create a series of HSF/GG hydrogels with distinct physicochemical profiles.
The composite hydrogels were thoroughly characterized in terms of morphology (via SEM), swelling behavior, degradation kinetics, rheological properties (storage/loss moduli, stress relaxation), and compressive mechanical strength. The incorporation of HSF with lower molecular weight enhanced water affinity and resulted in smaller and more uniform pore structures. Moreover, by adjusting the HSF content and hydrolysis degree, the viscoelastic properties of the hydrogels could be finely tuned, mimicking the mechanical behavior of soft biological tissues.
In vitro biocompatibility was assessed using NIH-3T3 fibroblasts. Live/dead staining and CCK-8 assays confirmed that all hydrogel formulations supported high cell viability, with no observable cytotoxicity. Cell spreading was also more favorable in HSF/GG hydrogels with moderately reduced SF molecular weight, likely due to improved matrix hydration and porosity.
Collectively, this study demonstrates a facile and reproducible method to fabricate biocompatible hydrogels with tunable mechanical and structural properties by manipulating the molecular weight of silk fibroin prior to gel formation. The resulting HSF/GG hydrogels exhibit high potential for use as scaffolds in soft tissue engineering, wound healing, and injectable biomaterials for minimally invasive therapies.

(0057)

Mechanically reinforced gellan gum hydrogel designed as a carrier for corneal endothelial cell transplantation

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Corneal endothelial dysfunction is a leading cause of vision loss worldwide, yet effective treatments are hampered by a shortage of donor tissue and risks of immune rejection. While gellan gum (GG) hydrogels are biocompatible and widely used for cell or drug delivery, their mechanical properties are insufficient for use as corneal substitutes. In this study, we developed a novel hydrogel by blending methacrylated gellan gum (MAGG) with GG and introducing lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) as a photoinitiator to enable photo-crosslinking.

The resulting GM/LAP hydrogel exhibited enhanced mechanical strength, suitable gelation temperature, and improved injectability compared to conventional GG hydrogels. Comprehensive physicochemical and mechanical assessments demonstrated that GM/LAP hydrogels possess favorable swelling behavior, degradation profile, and transparency close to that of native corneal tissue.

In vitro experiments with encapsulated corneal endothelial cells (CEnCs) revealed high cell viability, enhanced proliferation, and maintenance of corneal-specific gene expression. Furthermore, the photo-crosslinked hydrogel provided a supportive 3D environment for cell growth and matrix remodeling.

These results indicate that the GM/LAP hydrogel is a promising injectable cell carrier for corneal tissue engineering. Its enhanced mechanical properties and transparency closely resemble native corneal tissue, providing strong structural support. The hydrogel sustains high viability and proliferation of corneal endothelial cells, maintaining their specific function and gene expression. By offering a minimally invasive and biocompatible scaffold, GM/LAP may help overcome donor shortages and immune rejection. Overall, this approach has significant potential to improve outcomes in corneal endothelial cell transplantation.

(0058)

Impact of preservation techniques on the extracellular matrix of cell sheet constructs

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The extracellular matrix (ECM) is an essential component of all tissues and organs. It offers structural support as well as tensile strength, elasticity, and resistance to compressive forces. Beyond its mechanical roles, the ECM forms the physico-chemical environment where cells reside, conveying external signals that can trigger cell proliferation, differentiation, or death. Cell sheet (CS)-based engineered constructs, which rely heavily on ECM, have been proposed for repairing or replacing various tissues. For CS-based tissues to achieve widespread clinical use, it is crucial to maintain ECM integrity from fabrication to application. Although cryogenic and hypothermic preservation techniques present possible solutions, their effects on the structure of CS ECM remain incompletely understood. In this work, a direct comparison of the effects of cryogenic and hypothermic preservation on the ECM of CSs was performed by looking at putative changes in the composition and structure following both preservation methodologies. For each preservation method, the gold standard preservation solution was used. CSs of human adipose stromal cells (hASCs) were either stored at -196ºC using fetal bovine serum (FBS) with 10% (v/v) dimethyl sulfoxide (DMSO) or at 4ºC using the preservative hypothermosol (HTS). After 3 and 7 days of preservation, ECM structural integrity, mechanical properties, and relative protein abundance were assessed. Although proteomic analysis indicated that cryopreservation had no significant effect on the overall composition of the ECM, structural analysis suggests significant alterations induced by this technique, namely the disruption of collagen organization, which was not observed following hypothermic preservation. These structural changes were accompanied by alterations in mechanical properties, with cryopreserved cell sheets demonstrating a reduction in their elastic modulus. In contrast, hypothermic preservation had a milder effect on ECM structure, with preserved cell sheets maintaining matrix integrity and mechanical properties similar to the control before preservation. The observed alterations in ECM structure have important implications for the clinical translation of CS-based therapies. Although quantitative analyses revealed no significant deviations in ECM protein abundance, the pronounced structural changes induced by cryogenic preservation are likely to compromise the physiological functionality of CSs, with potential adverse effects on their therapeutic efficacy. This suggests that hypothermia may be the best alternative for preserving CS integrity and functionality from the fabrication site to to clinical application.

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POSTER PRESENTATIONS – Session 3
Advanced 3D Bioprinting & Marine/Sustainable Biomaterials

(0059)

Applying torque to the cell membrane using magnetic stimulation system enhance the functinoal maturation of cardiac organoids

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Mechanical forces play a pivotal role in cardiac development, inducing morphogenesis, lineage commitment, and functional maturation. Reproducing these biomechanical cues *in vitro* is essential to advance human heart researchers for both disease modeling and regenerative medicine. However, applying precise mechanical stimulation to three-dimensional (3D) multicellular systems remains a significant challenge in bioengineering. In this study, we developed and employed a novel Magnetic Torque Stimulation (MTS) system to apply controlled rotational mechanical stress to human pluripotent stem cell-derived cardiac organoids (COs).

The MTS system utilizes engineered magnetic beads conjugated with lectin to bind the glycoproteins of cell surface, which are actuated by a rotating uniform magnetic field to deliver torque forces. We generated COs from human induced pluripotent stem cells (hiPCs), comprising cardiomyocytes, fibroblasts, and endothelial cells to mimic the cellular complexity of the human heart. These organoids were integrated with magnetic particles and exposed to torque stimulation for 72 hours. The stimulation was applied at the different windonws considering the cardiogenesis of the heart; early and later stages.

Torque-stimulated COs exhibited substantial enhancements in structural, molecular, and functional maturation. Immunofluorescence and qPCR analyses revealed increased expression of mechanotransduction-associated genes, including PIEZO1, YAP1, LMNA, SYNE1 and, SYNE2, highlighting activation of force-responsive signaling pathways. Furthermore, key mesodermal (Brachyury, MESP1) and cardiac progenitor markers (ISL1, NKX2.5), as well as mature cardiac (cTnT, Cx43) and vascular (CD31, vWF, PDGFRß) markers, were significantly upregulated.

Functionally, torque-stimulated COs demonstrated improved electrophysiological properties, including synchronized contractions, increased conduction velocity, and elevated action potential amplitude. Metabolic profiling indicated a shift from glycolysis toward oxidative phosphorylation, suggesting enhanced bioenergetic maturation. The beating behavior of stimulated COs more closely resembled that of adult cardiac tissue, underscoring the physiological relevance of this approach.

Collectively, these findings show that magnetic torque stimulation is a potent and reproducible method to induce mechanotransduction, accelerate cardiac lineage specification, and promote the structural and metabolic maturation of cardiac organoids. This platform offers a valuable tool for modeling human heart development and function *in vitro* and presents a promising alternative to animal models in adult heart research and drug screening applications.

(0060)

Pressure-responsive conductive gelatin-alkali lignin hydrogels developed for meniscus repair

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The human meniscus experiences complex mechanical loads within the knee joint with unique biological and biomechanical characteristics, and is one of the tissues that frequently need medical intervention in the orthopedics requiring better integrating implants [1]. This study builds on our previously developed gelatin-alkali lignin hydrogels [2] for meniscus tissue engineering by highlighting their conductivity and pressure-sensing behavior, aiming to support their application in meniscus repair. The developed hydrogels were characterized for electroconductivity and impedance response under static and cyclic compression. The stable, composition-dependent conductivity and consistent impedance changes in response to compressive strain of the hydrogels highlight their dual functional potential as both structural and sensing elements, further supporting their unique features for load-adaptive, bio-interactive implants for meniscus regeneration.

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(0061)

3D printing of brushite-forming cu-substituted ß-TCP cements for bone tissue engineering

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Brushite cements features are excellent bioresorbability, osteoconductivity, and self-setting characteristics. Incorporation of relevant ions in brushite plays an essential part during the biological action course of the final cement, as well as their final mechanical properties [1]. Copper (Cu^{2+}) is a promising trace element known to enhance osteoblasts' activity and essential in new blood vessels formation [2]. 3D printing has emerged as a leading technology for producing porous structures with complex geometries, meeting the specific demands of bone tissue engineering. It offers precise control over fine architectural features such as interconnected porosity, pore size and distribution, and spatial heterogeneity—capabilities that are difficult to achieve with conventional fabrication methods. As well, the cements prefabrication ensures complete setting before in vivo application and enabling the formation of interconnected macropores. Hence, this study focused on 3D printing of brushite cements doped with Cu^{2+}, with the goal of enhancing both degradation behavior and bone regeneration. Cements containing 0.3 mol% Cu^{2+} were prepared by mixing ß-TCP powders with monocalcium phosphate monohydrate (MCPM) in a molar ratio of 1:0.6 [3]. Aqueous solution was prepared with 3 wt% phytic acid (inositol hexaphosphate) and 10 wt% poly(ethylene glycol), with liquid-to-powder ratio of 0.3 mL/g. The pastes were mixed and left to set for an additional 8 min before printing. The cement pastes were investigated regarding their setting reaction by XRD and isothermal calorimetry, while the hardening performance was assessed using Imeter measurements. The rheological properties were investigated to assess the printability. Printing accuracy resulting from the manufacturing process was studied by SEM and micro-CT, through the analysis of pore and filaments fidelity. The effect of both crystalline phase, ion doping, and pore structures on bone tissue regeneration were carefully studied.

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(0062)

3D printed pdrn/gelma bioink for muscle tissue engineering

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Volumetric muscle loss (VML) persists as a significant clinical challenge due to limited regenerative capacity of graft materials. 3D bioprinting offers a promising solution, but bioinks are needed to ensure both structural integrity and myogenesis. Here, we present a bioink incorporated with polydeoxyribonucleotide (PDRN), a deoxyribonucleic acid (DNA)-derived molecule with known regenerative and anti-inflammatory properties. Single-stranded DNA (ssDNA) derived from PDRN was conjugated with hyaluronic acid (HA) to form a hybrid ssDNA@HA complex to enhance cellular uptake and structural stabilization. This complex was incorporated into a gelatin methacryloyl (GelMA)-based bioink to fabricate 3D muscle constructs. *In vitro* studies showed that C2C12 myoblasts encapsulated in ssDNA@HA-GelMA exhibited high viability, increased proliferation, and upregulated myogenic markers. These results highlight the potential of this bioink in promoting functional muscle regeneration and offer a novel strategy for treating VML through advanced bioprinting techniques.

(0063)

Engineering a 3D hydrogel model to study tumor-stromal cell communication

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As our understanding of the complexity and heterogeneity of the tumor microenvironment deepens, the demand for innovative methods to dissect the diverse cellular interactions driving tumor progression and invasion becomes increasingly urgent. Here, we present a novel, customizable 4-well 3D culture chamber designed to investigate chemotactic behavior between various stromal cell types and a target cancer cell population. The system features a central well for tumor cells, surrounded by three equidistant wells reserved for stromal cells. Collagen type I was used to create a hydrogel for molecular diffusion studies. Diffusion of Rhodamine B-Dextran (10 kDa) and Albumin-FITC (66 kDa) through the collagen matrix was assessed, yielding diffusion coefficients (D) of 6.393 $\mu m^2/s$ and 0.6009 $\mu m^2/s$, respectively, aligning with the expected impact of molecular size on diffusion behavior. To replicate the intercellular communication characteristic of the tumor microenvironment, human stromal cells (hASCs, hDMECs, and hDFbs) were seeded into the peripheral wells, while VMM15 melanoma cells were placed in the central well. Migration was evaluated by measuring the area occupied by migrating cells within a four-quadrant (NW, NE, SW, SE) template. A significant directional migration of hASCs toward the central well ($p < 0.05$) was observed compared to control conditions lacking VMM15 cells. Similarly, hDFbs demonstrated enhanced migration toward VMM15 cells, with statistically significant increases observed in the NW ($p < 0.05$), SW ($p < 0.01$), and SE ($p < 0.05$) quadrants. Notably, no migration was observed for hDMECs or VMM15 cells themselves. Collectively, these results highlight the utility of the developed chamber as a powerful platform for investigating tumor-stromal interactions. Additionally, the findings underscore the supportive role of stromal cells in promoting tumor invasion through mechanisms such as cooperative invasion.

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(0064)

Engineering a biomimetic intestinal scaffold with tunable villi architecture via DLP 3D printing

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The human gut is a highly complex and dynamic organ, central to nutrient absorption, immune modulation, and drug metabolism [1,2]. Conventional *in vitro* models often fail to fully replicate the gut's architectural, mechanical, and biochemical microenvironment features, thus limiting their utility in translational research [3]. In this work, we present a proof-of-concept biomimetic scaffold designed to emulate villi-crypt structures of the human small intestine. The system was fabricated using digital light processing (DLP) 3D printing and PEGDA-based photopolymer resin. The 3D-printed scaffold is designed to comprise four zones, three of which contain villi of varying sizes, and a fourth that blends all three, enabling spatially resolved cellular interactions. Printing was conducted using optimized DLP parameters (50 µm layer height, 20 mW/cm^2 intensity, 3 s exposure), and ensuring high resolution and reproducibility [4]. The villi-crypt scaffold architecture was tailored to support compatibility with standard cell culture protocols. Scanning electron microscopy (SEM) confirmed the fidelity of the villi-crypt structures and the dimensional variation across zones (493 µm, 628 µm, and 778 µm). Additionally, surface modification with poly-D-lysine via electrostatic adsorption introduced a positively charged interface to promote cell adhesion.
The *in vitro* models were seeded with Caco-2cells to evaluate cell adhesion and cytocompatibility. Confocal microscopy confirmed epithelial monolayer formation and successful cellular attachment to the scaffold. After 21 days of culture, cells exhibited polarization. Live/dead assays and TEER measurements demonstrated the formation of a viable, functionally active epithelial layer, highlighting the system's potential for long-term intestinal studies.
Compared to conventional Transwell™ cultures, the scaffold offers superior imaging accessibility, scalability, and microenvironmental control. The use of commercial PEGDA resins enables rapid prototyping and future customization with functional biomaterials or patient-derived samples. This system also lays the foundation for co-culture integration, colorectal cancer (CRC) modeling, and personalized medicine approaches.

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(0065)

Gelatin-based and gellan gum-based bioinks for 3d (bio)printing of composite structures

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Knee menisci are crescent-shaped fibrocartilaginous structures, located between the condyles of the femur and tibia, which ensure axial load distribution, shock absorption and joint stabilization, while enabling nutrient distribution to the articular cartilage. Meniscal injuries, prevalent in both athletic and aging populations, are associated with chronic pain, impaired mobility and increased risk of osteoarthritis [1]. With conventional clinical treatments not providing long-term improvement, the need for tissue-engineered, biocompatible and biofunctional implants comprised of sustainable biomaterials has been investigated [2,3]. This preliminary study aims to develop a 3D-bioprinted composite structure using genipin-crosslinked gelatin-alkali lignin (Gel/AL) and high acyl (HAGG) and low acyl gellan gum (LAGG) blend bioinks assembled through poly-electrolyte complexation (PEC). Formation of Gel/AL and HAGG-LAGG PECs was assessed with QCM-D, zeta potential measurement and Fourier-Transform infra-red (FTIR) spectroscopy. Viscoelastic, tensile and compressive properties were evaluated with rheology and biomechanical testing. Genipin-crosslinked Gel/AL inks showed improved thermal stability and compressive performance. Both Gel/AL and GG blends showed high printability and adequate fiber fidelity upon 3D printing, while injectability studies proved low injection force, making the formulations appropriate for extrusion-based bioprinting (EBB) with cell-laden bioinks. *In vitro* cell viability and proliferation were investigated at different time points up to 7 days of culturing. Overall, this study demonstrated the combined cytocompatibility, biomechanical performance and suitability of Gel/AL and HAGG-LAGG PECs for extrusion-based bioprinting, while also highlighting their potential use in further meniscus tissue engineering and regenerative medicine applications.

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(0066)

Freeze-dried polysaccharide-based tubular constructs with enhanced biofunctionality via recombinant polypeptides

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Engineering versatile tubular structures is essential for advancing tissue engineering (TE) strategies requiring vascularization. This work proposes the development of 3D tubular constructs based on a synergistic blend of chitosan (CHT), alginate (ALG), and acemannan (ACE). These natural origin materials were selected for their combined benefits including physical stability, antibacterial properties, and the promotion of tissue healing [1-4]. Using freeze-drying technology on the blended solutions, flexible, dimensionally stable tubes featuring well-defined hollow interiors were successfully fabricated. The constructs demonstrated significant water uptake—absorbing approximately 20 times their dry mass—while maintaining structural integrity under physiological conditions over seven days. Morphological characterization by scanning electron microscopy (SEM) and micro-computed tomography (Micro-CT) confirmed the formation of uniform, porous architectures critical for effective nutrient and oxygen diffusion. To enhance bioactivity and mechanical performance, elastin-like recombinamers (ELRs) functionalized with the QK peptide—a vascular endothelial growth factor (VEGF) mimetic sequence—were incorporated into the tubular matrices. Although this modification reduced overall porosity, it preserved a pore size ≥100 µm and promoted an improved microenvironment that supports endothelial cell viability. Moreover, the architecture displayed notable flexibility and bending capability and suitability for suturing, suggesting their potential for dynamic environments where mechanical compliance is crucial and potential for practical surgical applications, where secure attachment and integration with biological tissues are essential. Furthermore, the sustained release of bioactive components, including ACE and ELRs, up to 7 days contributed to an improved endothelial cell proliferation. These findings demonstrate the potential of this customizable platform for the design of alternative vascular grafts, offering tunable mechanical properties, bioactivity, and dimensions suitable for cardiovascular tissue engineering applications.

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(0067)

Cross-linked elr hydrogel containing an embedded thermoresponsive coacervate that decouples elasticity from viscous relaxation for stem-cell mechanoregulation

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Introduction:Cell behaviour is dictated not only by the stiffness of the extracellular matrix (ECM) but also by how that stiffness relaxes in time; fast-relaxing (viscous) matrices promote spreading, proliferation and osteogenesis, whereas purely elastic matrices bias cells toward quiescence or adipogenesis. (1) Yet most synthetic hydrogels lock elasticity and viscosity together or require elaborate dynamic-covalent chemistries to separate them. Here we present a minimalist, three-component design that—so far as we are aware—is the first to decouple viscous and elastic responses using only orthogonal, readily implemented interactions. A permanently SPAAC-cross-linked elastin-like recombinamer (ELR) network provides a stable modulus, while dispersed, thermoresponsive coacervate droplets act as independent, tunable viscous dissipaters, thereby offering a clean handle to study how time-dependent mechanics steer cell fate.
Methods: Three recombinant ELRs were prepared. Two were derivatized (≈60 % of lysines) with azide (HRGD6-N_3) or bicyclo[6.1.0]nonyne (VKV-CC) for strain-promoted azide-alkyne cyclo-addition (SPAAC). The third, an oppositely charged diblock, was engineered to coacervate at 37 °C. Precursor solutions (50–200 mg mL^{-1}) were mixed at 4 °C to form relaxed, fully reacted hydrogels, with or without the diblock. Oscillatory rheology, stress-relaxation and creep-recovery were performed at 4 °C and 37 °C. Human mesenchymal stem cells (hMSCs, 7 000 cells cm^{-2}) were cultured on the gels; viability, spreading, YAP/TAZ localization and lineage markers were assessed.
Results: Introducing the diblock increased the loss modulus (G") by up to an order of magnitude between 0.1–10 Hz while leaving the storage modulus (G') unchanged, proving viscosity can be dialled in *post-synthetically* and *orthogonally* to stiffness. G' was set from ~0.1 to 10 kPa—covering brain to pre-calcified bone—by varying polymer content. The coacervate phase, dormant at 4 °C, activated at 37 °C to yield rapid stress-relaxation ($\tau_{1/2} \approx 30$ s) and fully recoverable creep. On adaptable gels, hMSCs showed >95 % viability, two-fold higher spread area, nuclear YAP/TAZ enrichment and up-regulated osteogenic markers compared with purely elastic controls, underscoring the pivotal role of matrix viscoelasticity in directing lineage commitment.
Conclusions: We deliver a first-of-its-kind ELR hydrogel that cleanly separates elasticity from viscosity without dynamic covalent motifs or complex processing, enabling precise dissection of how time-dependent mechanics govern cell fate. This versatile platform lays the groundwork for mechanobiology studies and the rational design of regenerative scaffolds whose mechanical signals can be tailored to drive specific cellular outcomes.

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(0068)

From cytotoxic to cytocompatible: tailoring pla/zno scaffolds via silane functionalization

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Integrating zinc oxide (ZnO) with poly(lactic acid) (PLA) presents a promising strategy for developing bioactive scaffolds for bone tissue engineering, as ZnO enhances PLA' s bioactivity. However, the degradation of the PLA matrix, triggered by the release of Zn^{2+} ions during processing, poses a significant challenge. This issue relates to the formation of acidic by- products and the rapid release of ions, which compromise cell viability in the culture medium. Surface modification of ZnO emerges as a potential approach to reduce the catalytic effect on the PLA chemical structure and the cytotoxic effects of ceramic particles while improving the compatibility of the composite. In this study, ZnO was functionalized via a wet chemical method using (3- aminopropyl) triethoxysilane (APTS), aiming to reduce Zn^{2+} release during melt processing and in vitro degradation. The functionalization was carried out with 30 wt % APTS dispersed in ethanol, buffered to a pH of 3.5–5, and followed by magnetic and ultrasonic stirring. The suspension was mechanically stirred for 3 hours at 70 ° C, then filtered, washed with ethanol, and dried at 100 ° C for 6 hours. The resulting ZnOSi was incorporated into PLA at 5 and 10 wt % using an internal mixer at 175 °C and 60 rpm for 5 minutes. Scaffolds with an 8 mm diameter, 3 mm height cylindrical geometry, and 400 µm pores were subsequently fabricated via 3D printing. Thermogravimetric analysis (TGA) indicated that PLA/ZnOSi composites exhibit an onset degradation temperature comparable to neat PLA and higher than PLA- ZnO composites without surface treatment, demonstrating improved thermal stability. Rheological tests supported these results, with treated samples showing a higher Newtonian viscosity plateau, suggesting reduced degradation during processing. Cytotoxicity assays using MC3T3 preosteoblastic mouse cells confirmed enhanced cell viability for scaffolds with ZnO surface modified filler. The APTS treatment effectively minimized medium acidification and Zn^{2+} ion release, promoting cell adhesion and proliferation in 5 wt % ZnOSi samples. These findings demonstrate that wet functionalization of ZnO with APTS successfully mitigates PLA degradation and improves cytocompatibility, supporting its potential use in bone tissue scaffold applications.

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(0069)
GELMA derived from fish by-products for 3d bioprinting

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The expansion of the fishery, aquaculture and processing industries has led to a significant increase in discards and by-products such as heads, skins, skeletons. This study focuses on the valorization of these by-products through the development of GelMA, a gelatin based material derived from fish skin waste. Fish-derived GelMA offers significant advantages over their bovine and porcine alternatives, including reduced risk of zoonotic disease transmission and fewer religious or ethical concerns. As a sustainable, high-value-added biomaterial, fish GelMA holds strong potential for biomedical applications. Its use as a bioink in 3D bioprinting enables the fabrication of customized scaffolds for the regeneration and repair of damaged tissues and organs, such as skin, cartilage and bone. These scaffolds can be further functionalized with bioactive compounds of interest, including drugs, cells or other tissue-specific agents, enhancing their therapeutic performance and functionality. In this study, gelatin was extracted from fish skins of various species, including yellowfin tuna (YT), skipjack tuna (SKJ), blue whiting (BW), turbot (T), hake (H) and Humboldt squid (HS). GelMA was synthesized using conventional methods by introducing methacryloyl groups onto the amine and hydroxyl functional groups of the dissolved gelatine through the dropwise addition of methacrylic anhydride. The resulting solutions were dialyzed and subsequently freeze-drying to obtain a semi-finished GelMA sponges and their degree of methacrylation was assessed by ^{1}H-NMR spectroscopy. A broad range of GelMAs was successfully obtained from non-cytotoxic gelatins derived from skins of marine discards and by-products. In terms of chemical properties, this study demonstrated a high degree of methacrylation (ranging from 90-100%) for all the synthesized GelMAs, with the lowest values for the GelMAs derived from hake and Humboldt squid. Then, the production of GelMA for 3D bioprinting was carried out by dissolving the sponges in PBS along with the photoinitiator LAP. Preliminary tests demonstrated their printability, resulting in mesh-shaped hydrogels after UV light crosslinking. These hydrogels were characterized based on their mechanical properties and biological response through *in vitro* cytotoxicity assays using NCTC-929 fibroblasts. Additionally, the hydrogels were successfully loaded with the antibiotic vancomycin. These findings suggest the potential use of these fish-derived GelMAs as bioinks for applications involving cells and other compounds of interest, including drug delivery.

(0070)

Extracellular matrix-based hydrogels from stromal vascular fraction cell sheets to support vascular network formation

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Vascularization remains one of the major challenges in tissue engineering (TE), limiting the viability and integration of engineered constructs. The stromal vascular fraction (SVF) of adipose tissue has emerged as a promising cell source for prevascularization strategies, due to its spontaneous vasculogenic capacity without exogenous growth factors supplementation [1]. This angiogenic potential is strongly influenced by the extracellular matrix (ECM) produced by SVF cells. ECM-derived hydrogels offer a biomimetic platform, preserving tissue-specific cues and supporting cell behavior. Here, we report the development and characterization of a hydrogel obtained from decellularized ECM of SVF cell sheets, aiming to support vascular network formation in vitro. SVF cell sheets were decellularized using standard methods. The ECM was lyophilized and enzymatically digested with pepsin. Decellularization efficiency was confirmed by DNA quantification, while collagen structural integrity was assessed by circular dichroism (CD). ECM protein content and complexity were analyzed via SDS-PAGE, western blotting, and mass spectrometry (MS). To obtain hydrogels with enhanced mechanical stability, gelatin and microbial transglutaminase were mixed with the ECM. Structural and biochemical characterization of obtained hydrogels included histological staining (H&E, Sirius Red/Fast Green), scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR) and Atomic Force Microscopy (AFM). Hydrogel transmittance, rheological behavior, and degradation kinetics were also evaluated. Finally, angiogenic potential was assessed via a tube formation assay using a co-culture of endothelial cells and stromal cells. The decellularization process efficiently removed nuclear material while preserving key ECM components. Protein analysis confirmed the retention of essential ECM molecules and extract complexity. The resulting gelatin-supplemented hydrogels were optically clear, structurally stable, and exhibited improved viscoelastic properties. The co-culture demonstrated robust cell adhesion, proliferation, and tubulogenesis on the hydrogels, confirming their biocompatibility and potential to support vascularization. In conclusion, we successfully developed a tissue-specific ECM-derived hydrogel with inherent angiogenic properties.The combination of structural fidelity, bioactivity, and mechanical performance highlights its potential for vascularized TE.

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(0071)
Micropatterned glycopeptide-based hydrogels that promote cellular alignment for cardiac repair

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Myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide. (He et al., 2023) While current therapies relieve MI symptoms, they fail to regenerate necrotic tissue resulting from the blockage of the blood supply that occurs during the ischemic event. Promising regenerative strategies include the use of hydrogel patches that stimulate cardiomyocyte proliferation, as well as the induction of cardiac repair mediated by different types of therapeutic agents. (Balbi et al., 2019; Gil-Cabrerizo et al., 2023) Herein, we propose the use of supramolecular hydrogels based on Fmoc-diphenylalanine-glucosamine-6-sulfate (Fmoc-FF-GlcN6S), designed to mimic the biofunctionality of glycoproteins found in the heart's extracellular matrix (ECM) and support cardiomyocyte contractility. (Castro et al., 2025) To further enhance the hydrogel's biomimetic properties, we incorporated a collagen-mimetic peptide, $(Pro\text{-}Pro\text{-}Gly)_{10}$, to better replicate the composition of cardiac ECM, which is predominantly composed of collagen types I and III. The hydrogel formulation has been optimized by tuning the concentrations of both the glycopeptide and collagen-like peptide. This hydrogel support can be micropatterned to guide cardiomyocytes alignment as observed in the native cardiac tissue. Comprehensive characterization of the hydrogel formulations includes assessments of chemical composition, mechanical stiffness (target range: 5–50 kPa), morphology, and biocompatibility. Our goal is to develop a versatile hydrogel capable of supporting cardiomyocyte alignment and growth, and that can be used as a platform for the promotion of cardiac regeneration.

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(0072)
Biocatalytic-induced supramolecular chirality in carbohydrate-based systems

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Chirality is an intrinsic property of biological systems. It influences different biological functions based on molecular recognition, enzymatic activity, and the self-assembly of biomolecules into higher-order structures.[1, 2] The study of chiral self-assembly is therefore crucial for understanding how living systems code and transfer stereochemical information to instruct function.[3, 4] Chiral self-assembly of peptides, proteins, and synthetic amphiphiles, has been extensively studied to establish guiding principles of the supramolecular chirality. On the other hand, carbohydrates that are stereochemically wealthier have been underexplored in this field.[5] Carbohydrates offer a chiral rich platform with multiple chiral centers and stereoisomers (e.g. epimers, enantiomers) that theoretically can form ordered assemblies with distinct optical and mechanical properties.[5, 6] In physiological environment, the assembly process is challenging to control because of the abundance of chiral molecules and possibility to form different out of equilibrium assemblies. To gather mechanistic insides into this process, we studied the ability of aromatic carbohydrates amphiphiles to form chiral assemblies upon an enzymatic action, i.e. under conditions of enzymatically-instructed self-assembly. We used alkaline phosphatase (ALP) to induce self-assembly upon dephosphorylation of two regioisomers, namely N-fluorenylmethyloxycarbonyl-glucosamine-1-phosphate (Fmoc-GlcN1P) and fluorenylmethyloxycarbonyl-glucosamine-6-phosphate(Fmoc-GlcN6P). A combination of real-time NMR, circular dichroism (CD), and polarized light microscopy characterization showed that dephosphorylation of Fmoc-GlcN6P is 1.6-fold more efficient than Fmoc-GlcN1P at low concentrations (5 mM). This difference diminishes with the concentration increase and disappears at concentration of 20 mM. Despite the different dephosphorylation rate, both isomers form right-handed helical fibers, as evidenced by SEM, CD (signals at 250–300 nm for Fmoc π-π transitions) and uniform birefringence observed under polarized light microscopy. Helical stability depended on the presence of salts: in water the helices were stable up to 80°C, whereas phosphate-buffered saline(PBS) destabilizes fibers, mirroring DNA's salt-dependent behavior. DOSY-NMR revealed transient ALP-substrate complexes during fiber nucleation, suggesting enzymatic control beyond simple dephosphorylation. In a summary, we demonstrate the potential of biocatalytic self-assembly as a tool in engineering chiral biomaterials with implications for adaptive soft matter and synthetic biology.

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(0073)

Sustainable drug delivery platforms based on starfish-derived biphasic calcium phosphate

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The proliferation of *Asterias rubens*, a prevalent echinoderm species, has become a significant ecological and economic concern in mussel aquaculture. The predatory behaviour of this starfish, particularly towards juvenile *Mytilus edulis*, has resulted in substantial biomass losses and consequent economic detriment to aquaculture operations (Agüera et al., 2021). For that reason, it is imperative to develop novel and sustainable mitigation strategies to address the impact of this species on bivalve cultivation, which may be done through harvest and valorization of that biomass. In this study we examine the potential of *A. rubens* ossicles to become a sustainable source for creating calcium phosphate-based materials, of relevance for biomedicine. In particular, our research aimed the production of biphasic calcium phosphate (BCP), a mixture of hydroxyapatite and ß-tricalcium phosphate (ß-TCP) known for its biocompatibility, for use in advanced drug delivery systems. To assess calcium phosphate formation, hydrothermal conversion of the ossicles calcium carbonate with phosphate solutions was established, with parameters selected for influence on the physicochemical properties of the resultant BCP (Marques C.F. et al., 2017): Ca/P molar ratios of 1.50, 1.59, or 1.62 at pH levels of 8.5 or 10.0. X-ray diffraction (XRD) and scanning electron microscopy (SEM) analyses were employed to characterize the crystallinity and morphology of the synthesized materials. At a Ca/P ratio of 1.50, synthesis at pH 8.5 predominantly yielded poorly crystalline hydroxyapatite, known for its biocompatibility and favourable interactions with biological tissue, and more ß-TCP phase. In contrast, synthesis at pH 10.0 under the same Ca/P ratio resulted in a notable improvement in crystallinity, as evidenced by increased peak intensities in XRD patterns. Cytocompatibility studies with SaOs-2 cells were performed to determine the most suitable conversion ratio for biomedical applications, which have indicated that the cells demonstrated a preference for the materials produced with a Ca/P ratio of 1.5 at pH 10. Additionally, the encapsulation efficiency of therapeutic molecules within the BCP matrix and controlled release profiles were explored. The ionic exchange properties of BCP facilitated the sustained release of pharmacological agents, presenting significant advantages for extended therapeutic efficacy, which may be critical in developing effective delivery systems that enhance patient compliance. In summary, this research highlights the viability of using *Asterias rubens* ossicles as an eco-friendly source for bioceramics-based advanced drug delivery systems, contributing to biomedicine progress while promoting sustainability of marine biological resources.

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(0074)

Fibrin-based immunomodulatory hydrogels incorporating maresin-1-loaded zein nanoparticles for enhanced wound healing

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Chronic wounds occur when healing is disrupted, remaining in the inflammatory phase. They significantly affect patients' quality of life and place a heavy burden on healthcare systems [1]. The present research work aims at developing a fibrin-based hydrogel incorporating immunomodulatory zein nanoparticles loaded with maresin-1 to modulate the immune response, resolve inflammation, and create a regenerative microenvironment for effective tissue repair, through M2 macrophage polarisation. A fibrinogen solution (2 mg/mL) was combined with maresin-1, empty zein nanoparticles, maresin-1-loaded zein nanoparticles, or a combination of maresin-1 and maresin-1-loaded zein nanoparticles. Thrombin (2 U/mL) was immediately added to initiate polymerisation, which proceeded for 20 minutes at 37 °C. Maresin-1 release was quantified via ELISA. Human macrophages, isolated from buffy coats of healthy blood donors through negative selection, were then cultured with the hydrogels to assess their M2 polarisation potential. The release assay demonstrated a sustained release of maresin-1 over seven days from fibrin hydrogels containing maresin-1-loaded zein nanoparticles, as well as from those combining free maresin-1 with maresin-1-loaded nanoparticles. LDH assay results confirmed that all hydrogel formulations were non-cytotoxic to human macrophages. Importantly, both hydrogel types—those with maresin-1-loaded nanoparticles and those combining free maresin-1 with the loaded nanoparticles—markedly promoted macrophage polarisation toward the M2 phenotype, outperforming free maresin-1 and empty nanoparticles. These findings underscore the therapeutic promise of these hydrogel systems in modulating immune responses. Fibrin hydrogels incorporating maresin-1-loaded zein nanoparticles were successfully synthesised. Following seven days of culture with primary human macrophages, cell morphology remained intact, indicating excellent biocompatibility. Moreover, these hydrogels effectively directed macrophage polarisation towards the M2 phenotype, promoting anti-inflammatory and pro-regenerative responses.

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(0075)

Forest biomass-derived biopolymers for enhancing antioxidant, flexibility, and antibacterial activity of poly(lactic acid) films targeting safer applications.

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Bio-based and biodegradable polymers derived from renewable sources, such as poly (lactic acid) (PLA), exhibit suitable physicochemical properties and biocompatibility, leading to significant applications in biomedical fields, including implants, tissue engineering, sutures, and drug delivery systems [1, 2]. However, depending on the application, PLA has certain drawbacks, such as low degradation rate, acidic degradation by-products, limited flexibility, and minimal antibacterial action [3]. To address some of these drawbacks, this work adopts an innovative approach by valorising biopolymers sourced from natural resources, preferably isolated from forest biomass, to produce sustainable PLA-based films with enhanced properties. The resulting bio-based films produced by solvent casting demonstrated good dimensional stability and reproducibility. Additionally, incorporating natural biopolymers improved the films' ultraviolet (UV) radiation blocking ability, antioxidant activity, and mechanical properties, particularly by increasing their elasticity. Furthermore, this strategy also enhanced the antibacterial activity of the bio-based films, resulting in a reduction of the bacterial growth, which is especially relevant for packaging films and membranes in health-related applications. In addition, these functional improvements can be attributed to the interactions between PLA and the added biopolymers. Overall, these bio-based films exhibit promising characteristics suitable for applications requiring safer and more sustainable materials.

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(0076)
Supercritical co_2 decellularization of codfish skin FOR ECM-based biomaterials

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In tissue engineering, marine biomass is increasingly explored as source of biomaterials for developing extracellular matrix (ECM)-based scaffolds. One promising approach involves the decellularization of fish tissues to eliminate cellular components while preserving the ECM's native structural and biochemical features, enabling attaining biomimetic scaffolds. This study investigates the use of supercritical carbon dioxide ($scCO_2$) with ethanol as a co-solvent to decellularize codfish (*Gadus morhua*) skin - proposing a detergent-free environmentally friendly alternative to traditional chemical decellularization methods. Various treatment protocols, differing in exposure time and pressure cycles, were assessed for their effectiveness in cell removal and ECM preservation using (immuno)histochemistry, scanning electron microscopy, and quantitative biochemical assays. Further characterization through FTIR-ATR, thermogravimetric analysis, and mechanical testing provided insight into the physical and chemical properties of the obtained scaffolds. Biocompatibility was assessed by culturing HaCaT keratinocytes on these matrices for up to five days. Among the tested protocols, the one consisting of a 1-hour treatment followed by four 30-minute pressure cycles, showed the best balance of effective decellularization and ECM preservation, supporting robust keratinocytes attachment and growth. These results underscore the potential of $scCO_2$ processing as a viable technique for creating marine-derived scaffolds suitable for regenerative medicine applications.

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(0077)

Modified gellan gum nanoparticles as drug delivery vehicles

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Cardiovascular diseases are the leading cause of mortality worldwide, namely, heart failure (HF) resulting from ischemic heart disease and myocardial infarction (MI). Despite the substantial socioeconomic burden, current treatment options remain limited, with heart transplantation being the main treatment available in advanced stages of HF[1]. MI leads to the irreversible loss of functional cardiomyocytes and fibrotic tissue formation, impairing cardiac function[2]. A strategy to induce the regeneration of the myocardial tissue is the use of paracrine modulators in the form of proteins. However, their local delivery and retention at the target site is difficult, showcasing the necessity to develop sustained local delivery systems able to circumvent these hurdles. We are testing cell-free delivery vehicles using gellan gum (GG), a biocompatible natural polysaccharide. GG-based nanoparticles (@150nm average diameter) were produced following a procedure previously published by our group[3] and fluorescently labelled with FITC (FITC-GGnps) to enable cell tracking. Their physicochemical properties, including size, zeta potential and polydispersity index, were monitored over 7 days using DLS for both types of GGnps (i.e., with and without FITC). Morphological analysis was performed using SEM, and nanoparticles' stability was assessed in water, culture medium, and PBS (over the same period). Our results show that both GGnps and FITC-GGnps are stable under physiological conditions over the tested timeframe. Biocompatibility studies show that FITC-GGnps were non-toxic up to a concentration of 200µg/mL. In parallel, we are synthesizing sulfated GG nanoparticles (s-GGnps) that can capture and preserve growth factors in their bioactive conformation for extended periods of time – a characteristic of the sulfated glycans present in the extracellular matrix of living tissues. This approach represents a promising step toward minimally invasive, cell-free therapeutic strategies for myocardial repair.

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(0089)

Marine-based injectable platforms: development of cryogels for cartilage repair using fish collagen, chondroitin sulfate and hyaluronic acid

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The application of marine-derived biomaterials is becoming increasingly popular as a biocompatible and eco-friendly alternative to the use of mammalian compounds in regenerative medicine. The current study investigates the prospect of creating injectable cryogels for cartilage regeneration based on three marine-sourced biopolymers — collagen, chondroitin sulfate (CS), and hyaluronic acid (HA) —. Collagen and CS were extracted from *Prionace glauca* skin and cartilage, respectively, while HA was produced by bacterial fermentation using marine peptones as protein substrate. After examining a rigorous physicochemical characterization of isolated compounds, several hydrogel formulations were prepared through mixing biopolymer solutions at low temperature, varying concentrations and ratios, with electrostatic intereactions being further complemented by covalent crosslinking approaches. Mechanical cohesiveness and injectability of resulting systems were evaluated in response to formulation variables. FTIR analyses confirmed the identity of the materials, revealing characteristic signals such as amide bands in collagen, sulfate vibrations in CS, and a carboxylate peak around 1610 cm^{-1} in HA. Circular dichroism confirmed the preservation of the triple-helix structure in shark-derived collagen. Rheological assessment demonstrated shear-thinning behavior in both collagen and HA, with increased viscoelasticity at higher HA concentrations. The sulfation level of marine CS was evaluated using the DMMB assay, which showed significantly higher values (1.26 ± 0.32 µg/mL) compared to bovine-derived CS. Zeta potential analysis revealed a strong negative surface charge for HA (–45.1 mV), and a moderately negative value for CS (–20.2 mV), supporting their electrostatic stability. Additionally, marine-derived collagen showed a positive zeta potential of +19.4 mV, supporting the referred electrostatic interactions between the three components. The formulation method allowed for the adjustment of properties of cryogels such as cohesiveness and mechanical stability in PBS, with a direct effect on injectability. Blending marine-derived collagen, CS, and HA in predetermined ratios resulted in hydrogels of adjustable nature and potential application as injectable scaffolds for minimally invasive articular pathology treatment. Altogether, this research emphasizes the functional capabilities of marine biopolymers, aligned with circular bioeconomy approaches through valorization of fish by-products, and supports their use as sustainable alternatives in the design of next-generation regenerative materials.

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(0079)

FUNCTIONALIZATION OF PLGA/β-TCP SCAFFOLDS WITH SILK FIBROIN FOR APPLICATION IN BONE REGENERATIVE MEDICINE: A TOPOGRAPHIC ANALYSIS

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The functionalization of scaffolds intended for bone regenerative medicine (BRM) has proved to be a promising approach, since it can maximize the efficiency of the regenerative process conducted by scaffold-based BRM strategies. However, there are still uncertainties regarding the influence of this functionalization on the topographical surface characteristics, which also represent a determining factor in the cytocompatibility and regenerative potential of these strategies. To evaluate the influence of a functionalization process with silk fibroin (SF) on the surface topographical parameters of printed PLGA/β-TCP scaffolds with potential application in MRO. To this end, SF solutions in three concentrations (4.7%, 0.47% and 0.047%) were applied to the surface of PLGA/β-TCP scaffolds printed using the Fused Deposition Modeling technique. After treatment with methanol and dry, samples of the SF films were removed for characterization by X-ray diffraction. For topographical characterization, PLGA/β-TCP scaffolds coated with SF and without the coating were characterized by optical profilometry. X-ray diffraction analysis of silk fibroin films revealed distinct structural patterns depending on the methanol treatment. Untreated films exhibit a typical configuration of random chains, characterized by an amorphous structure with no crystalline peaks observable in the X-ray graph. In contrast, the X-ray pattern of the films treated with methanol for 1 hour showed crystallization peaks at 14.5° (s), 17.3° (ms) and 26.0° (s), indicating the formation of Silk I crystals. This change in the secondary structure of fibroin films increases their insolubility in water and results in a more stable coating, making them more suitable for use in medical devices. Optical profilometry analysis showed that the higher the concentration of silk fibroin coating, the lower the roughness (-68%), valley depth (-53%), surface area (-54%) and flooded surface volume (-72%). However, all surfaces showed isolated sharp peaks or valleys (kurtosis > 3) and intermediate texture isotropy (~0.5). The results show that the functionalization process of PLGA/β-TCP scaffolds printed with SF had a significant influence on surface topographical aspects, producing a distinct morphology in relation to the original roughness and potentially influencing the cytocompatibility process. Additional in vitro cytocompatibility analyses need to be conducted to characterize this influence.

(0080)

Rheological influence of meniscus-derived decellularized extracellular matrix on hyaluronic acid hydrogels for biomedical applications

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A matriz extracelular descelularizada (dECM) serve como uma plataforma versátil para sistemas de entrega em aplicações biomédicas, capaz de incorporar e liberar células, moléculas de sinalização e produtos farmacêuticos projetados para modular o microambiente de um tecido/órgão alvo. Além disso, exerce efeitos modulatórios intrínsecos, preservando componentes estruturais e moléculas de sinalização que regulam processos celulares críticos. Para permitir a administração minimamente invasiva de dECM, ele deve ser integrado a um veículo compatível com a administração injetável. Um dos principais veículos empregados na pesquisa e na prática clínica é o ácido hialurônico (AH), conhecido por suas excepcionais propriedades biológicas e reológicas. Apesar do potencial e alto desempenho dos sistemas injetáveis à base de hidrogel de HA, a literatura ainda carece de estudos abrangentes que demonstrem conclusivamente como a incorporação de dECM pode influenciar suas propriedades reológicas e, consequentemente, o impacto nos métodos de administração. O objetivo deste estudo foi avaliar a influência da dECM derivada do menisco (mdECM) no comportamento reológico de hidrogéis de AH. O mdECM foi obtido por meio do protocolo de descelularização para meniscos suínos descrito por Xu et al. (2017), seguido de moagem criogênica para produzir fibras em escala nano/micrométrica. Posteriormente, concentrações variadas de mdECM (0,2, 0,3 e 0,5 mg/mL) foram incorporadas em hidrogéis de 20 mg/mL de AH (2,1 MDa). As amostras foram submetidas a testes reológicos sob regimes de fluxo contínuo e oscilatório e foram comparadas a um grupo controle sem mdECM. Os resultados demonstraram que todos os hidrogéis exibiram comportamento viscoelástico linear sob deformações moderadas (até 100%), indicativo de uma rede polimérica estável com interações moleculares robustas. Além disso, foram observadas semelhanças na pseudoplasticidade e tixotropia - críticas para aplicações injetáveis - garantindo fluxo controlado e retenção de forma in situ. As análises Tan-δ revelaram que a incorporação de mdECM reduziu significativamente a razão G"/G', mudando o comportamento predominante de viscoso para viscoelástico. Essa transição pode ser atribuída, pelo menos em parte, à integração entre os componentes da dECM (colágeno e glicosaminoglicanos) e a matriz polimérica do AH. Em conclusão, o mdECM não alterou as características pseudoplásticas e tixotrópicas intrínsecas do AH, tornando esses hidrogéis compostos candidatos promissores para sistemas injetáveis na medicina regenerativa musculoesquelética.

(0081)

Biomedical potential of chondrosia reniformis collagen for scaffold development in tissue engineering

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Among the various biopolymers available, collagen stands out as an effective material for cell culture scaffolds aimed at regenerating diverse tissue types. Although mammalian by-products remain the primary industrial source for biomedical applications, concerns related to zoonosis and religious/ cultural restrictions have driven the search for alternative sources. Collagen derived from marine organisms has emerged as a promising and sustainable alternative, though it remains largely underutilized. In particular, collagen from Chondrosia reniformis, a marine sponge that can be cultivated in IMTA systems, was previously studied for skin care applications. The aim of this study was to develop porous scaffolds from C. reniformis collagen and evaluate their suitability as templates for cell culture, with a focus on engineering skin, cardiovascular tissue and cartilage, ultimately promoting the chondrogenic differentiation of stem cells. Collagen was crosslinked using EDC, genipin and glutaraldehyde, and then freeze-dried to fabricate the scaffolds. Their physicochemical and mechanical properties were characterized using SEM, microCT and rheometry, alongside assessments of degradation and swelling behaviour. Genipin emerged as the most promising crosslinker due to its low cytotoxicity and the formation of scaffolds with larger pores, which were favourable for cell culture. The biological performance was evaluated through in vitro cell culture experiments, assessing cytocompatibility with ATDC5 (chondrogenic cell line), BJ (fibroblasts), EA.hy926 (umbilical vein cell line), and ASCs (adipose-derived stem cells), as well as the potential to support the chondrogenic differentiation of ASCs. Genipin-crosslinked scaffolds were found to be well-suited for tissue engineering applications, as they promoted increased cell metabolism and proliferation, and supported early chondrogenic differentiation of ASCs even under basal conditions. These findings further highlight the versatility of C. reniformis collagen for biomedical use, particularly in cartilage regeneration, positioning it as a promising alternative for the development of future human regenerative therapies.

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(0082)

Engineering a vascularized 3D model of the spleen red pulp

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The spleen is a vital secondary lymphoid organ with a highly organized architecture, composed primarily of white pulp (WP) and red pulp (RP). The RP, which constitutes the majority of the splenic mass, is essential for filtering blood, removing senescent or damaged erythrocytes, and initiating immune responses [1]. Structurally, the RP consists of a loose reticular network of fibroblasts, endothelial cells, and extracellular matrix (ECM). Together, these components form a discontinuous, open circulatory system. In this system, blood exits terminal arterioles into splenic cords rather than direct venule connections, allowing erythrocytes to interact closely with macrophages. This arrangement enables the efficient clearance of abnormal cells and blood-borne pathogens. However, replicating the RP's specialized microenvironment and vascular dynamics in vitro remains a significant challenge, and there are few models that faithfully recapitulate its structural and functional complexity [2].

To address this gap, we are developing a spleen-like hydrogel-based 3D matrix integrated with spleen vascular units (S-VUs). sdECM-based hydrogels were successfully formed via di-tyrosine visible light photocrosslinking [3], with less than 30 sec of visible light irradiation being sufficient to generate hydrogels at 1 wt.% dECM and low photoinitiator concentration (0.25/2.5 mM/mM Ru/SPS). Hydrogels were tested as matrices for 3D culture of human splenic fibroblasts (HSF), which exhibited high viability, proliferated, and spread over time. S-VUs were formed as previously described [4], using different cell types/ratios, including spleen microvascular endothelial cells (SMEC) or endothelial colony-forming cells (ECFC) combined with HSF. Size/morphology, metabolic activity, endothelial organization, ECM production, and angiogenic sprouting potential were assessed. Optimal results were observed at an ECFC/HSF ratio of 1:5, which promoted endothelial cell retention and favourable cell/matrix organization. Upon embedding in sdECM hydrogels, the S-VUs formed HSF-supported, lumenized capillary networks.

Further studies will refine the hydrogel composition and incorporate additional cell types to enhance biomimicry. Ultimately, our goal is to develop a biomimetic 3D model that faithfully recreates key structural and functional properties of the spleen RP, providing a more physiologically relevant platform for spleen research.

(0083)

Therapeutic potential of bioactive glass nanoparticles in spinal bone regeneration

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Bioactive glass (BG) has gained considerable attention in bone tissue engineering due to its excellent bioactivity, osteoconductivity, and capacity to bond with surrounding bone. However, its limited osteoinductive capability remains a challenge for more effective bone regeneration. To address this, we functionalized the surface of BG particles with Bone Morphogenetic Protein-2 (BMP-2), a well-known osteoinductive growth factor, to develop a composite system with enhanced regenerative performance. To facilitate delivery and retention at the defect site, the BMP-2-functionalized BG (BG/BMP-2) was subsequently incorporated into an injectable, biodegradable hydrogel matrix, enabling localized application and sustained release within the target tissue. BMP-2 was immobilized on the BG surface via dopamine to preserve protein bioactivity and ensure controlled release. The resulting BMP-2-functionalized BG (BG/BMP-2) was characterized through scanning electron microscopy (SEM), which revealed morphological changes on the particle surface. In addition, to confirm the sustained release of BMP-2 under physiological conditions, the release pattern over time was evaluated and the resulting pH change was also investigated. *In vitro* studies were performed using bone marrow-derived mesenchymal stem cells (BMSCs). BG/BMP-2 demonstrated excellent cytocompatibility, as confirmed by cell proliferation assays. Furthermore, osteogenic differentiation was significantly enhanced in the BG/BMP-2 group compared to BG alone, as demonstrated by increased alkaline phosphatase (ALP) activity, upregulated expression of osteogenic markers (*OCN*, *COL1*, *OPN*). *In vivo* evaluation, BG/BMP-2 was incorporated into a biodegradable hydrogel matrix and applied to a critical-size spinal bone defect model in rats. Histological analysis after 8 weeks revealed substantial new bone formation in the BG/BMP-2 group, along with better defect bridging and matrix remodeling compared to BG or hydrogel-only controls. Histological staining demonstrated mature bone tissue integration and vascularization at the regeneration site. These results demonstrate that BG/BMP-2 composites can provide both structural support and biochemical cues necessary for effective bone regeneration. The hydrogel-based delivery system further facilitates localization and retention of the composite at the defect site, enhancing therapeutic outcomes. In conclusion, the BMP-2-functionalized bioactive glass embedded in a hydrogel matrix represents a promising strategy for spinal bone regeneration. This composite scaffold system shows potential for clinical translation in treating complex bone defects that require both osteoconductive and osteoinductive properties.

(0084)

Osteoinductive bioactive glass-poly (mpc-co-butyl methacrylate) composites for mandibular bone regeneration

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Mandibular bone defects, particularly in the molar region, present significant clinical challenges due to their complex anatomical structure, functional demands, and limited regenerative capacity. Effective reconstruction in these areas requires biomaterials that can not only support bone regeneration but also integrate seamlessly with the surrounding tissue. Bioactive glass (BG) has been widely utilized in bone tissue engineering owing to its excellent bioactivity, osteoconductivity, and strong bonding ability with bone. However, its surface properties often lead to nonspecific protein adsorption and suboptimal cellular responses, which may limit its regenerative potential in complex oral environments. To address these limitations, we developed a novel composite system by combining BG with poly (2-Methacryloyloxyethyl phosphorylcholine-co-butyl methacrylate) (PMB), a zwitterionic copolymer known for its superior biocompatibility, protein-repellent characteristics, and ability to promote cell adhesion and proliferation. The resulting BG/PMB composite was fabricated via surface immobilization of PMB onto BG particles and was thoroughly analyzed in terms of surface morphology, pH changes under physiological conditions. To facilitate localized delivery and retention within the defect site, the BG/PMB particles were incorporated into an injectable hydrogel matrix. In addition, a swelling test of the hydrogel was conducted to evaluate its physicochemical stability and fluid absorption capacity, which are critical parameters for *in vivo* performance. *In vitro* studies using bone marrow-derived mesenchymal stem cells (BMSCs) revealed that the BG/PMB composite exhibited excellent cytocompatibility, supporting cell attachment and proliferation. Moreover, osteogenic differentiation was significantly enhanced, as evidenced by elevated alkaline phosphatase (ALP) activity, upregulation of osteogenic gene markers compared to BG alone. These results indicate that PMB functionalization effectively improves the biological performance of BG. To validate *in vivo* efficacy, the BG/PMB composites were applied to a rat mandibular molar defect model. Micro-CT and histological analyses conducted after 8 weeks demonstrated significantly improved new bone formation, defect bridging, and bone–material integration in the BG/PMB-treated group relative to control groups. In conclusion, the BG/PMB composite represents a promising biomaterial for mandibular bone regeneration, particularly in the molar region where mechanical and biological requirements are demanding. Its enhanced biocompatibility and osteoinductive properties suggest potential broader applications in oral and maxillofacial reconstructive procedures.

(0085)

Injectable TGF-β3-Loaded Hyaluronic Acid Hydrogel Enhances Cartilage Regeneration via Controlled Release and Microfracture-Induced Stem Cell Recruitment

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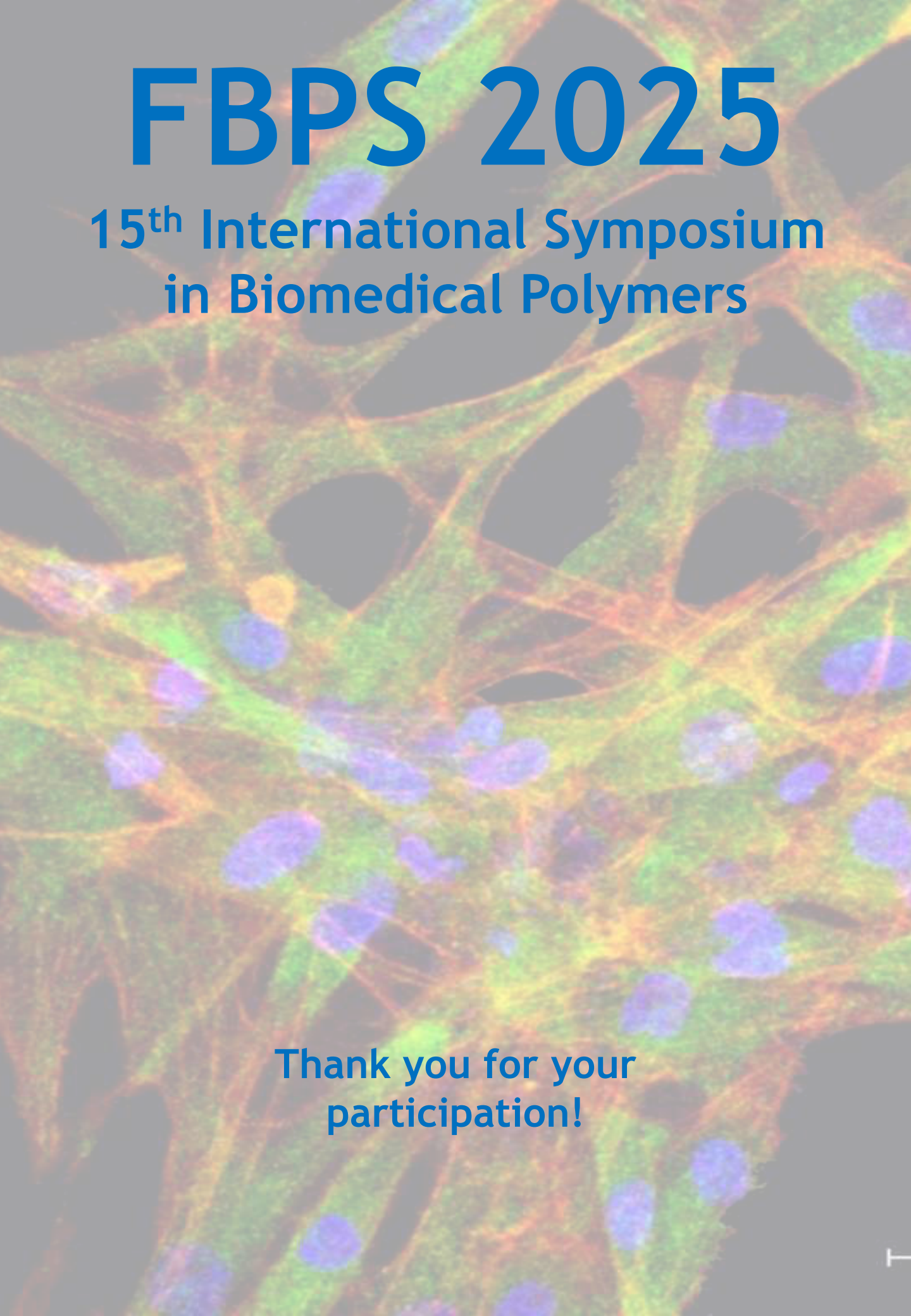
Cartilage injuries pose a significant clinical challenge due to their limited intrinsic healing capacity. To address this, we developed an injectable crosslinked hyaluronic acid (HA) hydrogel incorporating transforming growth factor-beta 3 (TGF-β3), termed HAT.
This study evaluated the hydrogel's physicochemical characteristics, biocompatibility, and therapeutic efficacy in promoting cartilage regeneration.
The HAT hydrogel displayed an interconnected porous structure (avg. pore size ~115 μm), excellent injectability, tissue adhesion, and sustained TGF-β3 release over 28 days.
In vitro assays confirmed high cell viability, enhanced rabbit bone marrow-derived mesenchymal stem cell (rBMSC) proliferation, and chondrogenic differentiation.
In vivo studies in a rabbit chondral defect model demonstrated that HAT significantly improved tissue integration, extracellular matrix formation, and cartilage repair, particularly when combined with microfracture (MFx)-induced stem cell recruitment.
Histological analysis revealed superior regeneration of hyaline-like cartilage and reduced inflammatory response. These findings support HAT as a promising platform for minimally invasive cartilage repair.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