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第二届国际先进医学工程大会

ABSTRACTS 摘要集

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College of Materials Science & Engineering, Hunan University

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Symposia 1
Plenary speaker abstract

Opportunities and Challenges in Aging Bone Regenerative Materials

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The repair and reconstruction of aging bone defect is a difficult problem because of the deteriorative regenerative capacity. Biomaterial-based treatments are one of the important strategies for bone repairing. Improving the osteogenic activity and bone integration ability of the materials, as well as how to adapt to the needs of minimally invasive surgery in aging patients, are the challenges that aging bone regenerative materials need to face. After implantation, biomaterials can not only provide a structural framework to support, but also facilitate the attachment and migration of host stem and progenitor cells, and play an important role in driving the differentiation of mesenchymal stem cells. Furthermore, traditional calcium-phosphates biomaterials showed a novel function of reducing bone loss during long-term implantation in aged animals. Therefore, it is necessary to decode some biological effects of bone-repairing materials from the view of materiobiology, which can improve bone regeneration.

Key Words: materiobiology, bone regeneration, aging, calcium phosphates

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Engineering Micro-Physiological Systems (MPSs) as NAMs for Drug Development

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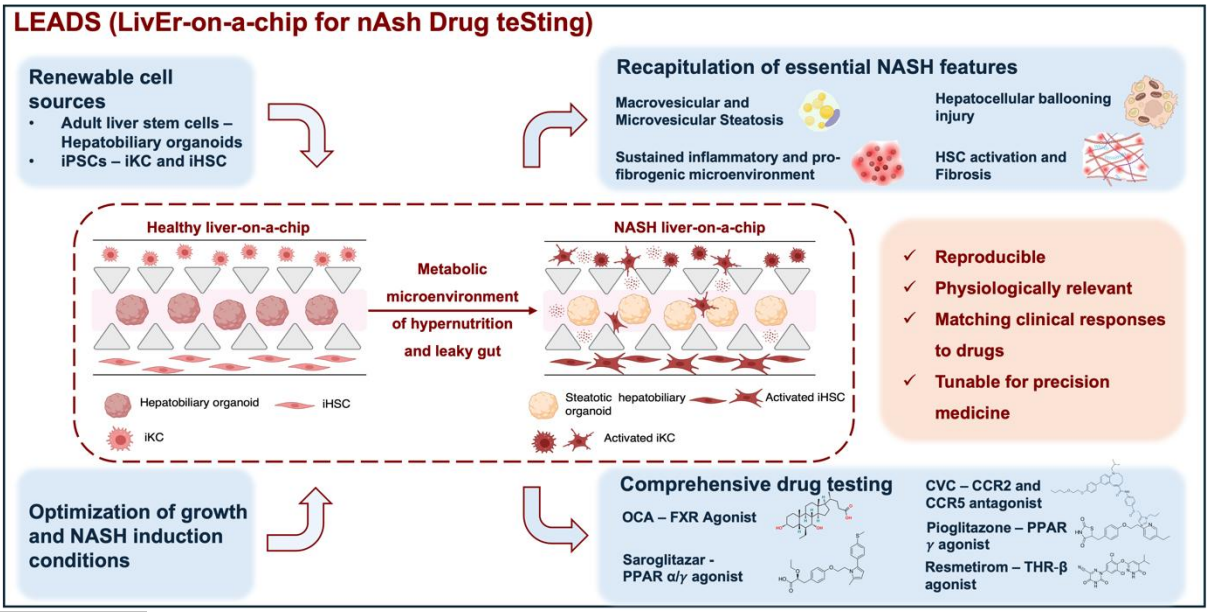
"The FDA's animal testing requirement will be "reduced, refined, or potentially replaced" with so-called New Approach Methodologies, or NAMs data, which include the use of AI-based models to predict a drug's behavior as well as side effects and testing on human organ-like structures made in a laboratory." – Reuters April 10, 2025 [1] Developing human organ-like structures with proper physiological and pathological functions is useful in various stages of the drug development pipeline. Using metabolic dysfunction-associated steatotic liver disease (MASLD) as an example, I will illustrate our efforts to engineer MPSs of different complexity to support each specific application. For MASH drug efficacy, a full disease model (LEADS) with all the relevant cell types is constructed to mimic liver sinusoids stressed by MASH environment [2] of steatosis, inflammation and fibrogenesis. For drug MOA studies and biomarker discovery, a reduced model of lipid droplet mechano-chemical dynamics is developed to map the corresponding nodes in metabolic network and relevant functional modules affected by the drugs. Engineering design considerations [3] will be discussed to construct the minimally sufficient MPSs recapitulating the disease progression, while maintaining the robustness and throughput.



Key Words: liver disease models, mechanobiology, organoids, micro-steatosis, macro-steatosis

Acknowledgements: Mid-Size Centre grant from National Research Foundation

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The Manufacture of Whole Organ on Demand

Joseph Vacanti
Massachusetts Gen Hospital

As a clinical surgeon, let me share this journey through personal stories. The advancing regenerative medicine requires close interdisciplinary collaboration. Drawing from decades of my research experience, I shared insights into personalized regenerative organ development as a solution to organ transplant shortages and outlines future directions for the field. Due to witnessing patients' urgent need for liver transplants, my initial research focused on implanting biodegradable polymer scaffolds to repair liver tissue defects. However, this approach demonstrated limitations in supporting larger organ structures due to insufficient oxygen and nutrient diffusion. To address this challenge, our team developed branching vascular systems mimicking natural circulatory networks, enabling effective nourishment of all cellular components in engineered tissues. A landmark achievement occurred in 1997 when the BBC featured their groundbreaking work-the successful cultivation of a living ear structure on murine models. This widely publicized breakthrough not only popularized tissue engineering concepts but also coincided with the emergence of stem cell biology as a fundamental pillar for tissue regeneration strategies. Subsequent advancements in 1998 incorporated computational fluid dynamics to replicate physiological blood flow patterns, combined with early 3D printing technologies to create high-precision vascular architectures in hepatic and other tissues. These innovations laid crucial groundwork for engineering vital organs.

Towards Next Generation Bioresorbable Implants

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Bioresorbable implantable medical devices are intended to facilitate regeneration of tissue using the body as a bioreactor. They and their metabolic byproducts are necessarily non-toxic and completely excreted. They are indicated for clinical problems presenting a defect of tissue that is large in volume, distributed in a challenging way, involves considerable donor morbidity for autologous reconstruction or introduces a high failure rate for alloplastic reconstruction. These are represented in several specific clinical contexts including large bone defects in the appendicular skeleton, bone defects of the craniofacial skeleton and breast volume replacement. Challenges in translation of bioresorbable implants include scaling up, hostile clinical environments (including infection and radiotherapy) and composite defects include whole organs.

The authors have undertaken large animal and clinical trials of implantable bioresorbable devices covering all of these clinical contexts. This presentation will present the contemporary science that informs future directions in bioresorbable devices. This includes never seen before results of systematic histological examination of explanted specimens and biopsies from animal and human studies that serve to outline the cellular processes involved in tissue regeneration. It also informs the next steps that should be taken to optimize next generation bioresorbable devices to improve the rapidity of tissue regeneration and work towards multi-phasic implants that are capable of regenerating multiple tissue types in a single device.

Key Words: bioresorbable, implant, reconstruction, defect

The Future of MedTech in Asia

Prof Teoh Swee-Hin;

College of Materials Science and Engineering, Hunan University, China

MedTech industry [1] is expanding rapidly from tissue engineering/regenerative medicine and to AI in data analytics and assisting surgeons in diseases diagnostics. The talk will begin with lessons from nature- how snails and salamander regrow their organs after amputation of the body and limbs. As early as 1965 where 29 dogs were used for tissue engineering of heart valves but fail dramatically emphasizing the role of biomaterials in regeneration and the methods of manufacture became very important. Then in 2003, the integration of medical imaging, 3D printing and bioresorbable polymers such as polycaprolactone where more than 200,000 lives have been saved by this technology that allows cells to create home, proliferate and express their cellular matrices and over time the PCL degrades into carbon dioxide and water and leaving no foreign chemicals to invoke any long-term host tissue response. The design of scaffolds to allow early vascularization has been key in the success. Without the partnership of engineers and clinicians to address the surgical method and the scaffolds design in vascularization, many first in man of large tibia (>150mm) regeneration will not be possible. However, there are still many challenges facing the MedTech industry in Asia. Training a new breed of graduates to LEAD and CREATE NEW MedTech Industries that integrates Medicine and Engineering with an Entrepreneurship Character calls for a new paradigm shift in education – training graduates to Lead rather than Feed has become very important. Taking the Harvard studies on early child brain development it is clear that learning 1) involves synapses firing, 2) involves multidisciplinary network; 3) learning cannot be compartmentalized 4) learning is best by doing- by experience and 5) creativity is directly related to the rapid synapses firing of the brain.. There is a growing concern that Asia is aiming for top publications such as Nature and Science but trailing far behind west in entrepreneurship. Some of the challenges faced by Asia include 1) Lack of Clinician-Engineer Partnerships; 2) Lack of Interdisciplinary Talent Pool-Each working in Silos 3) Innovations Hampered by Clinicians having No Time for Research; 4) Different Regulatory Requirements in each Region Leading to few Clinical Trails. The need to form a strong Clinician-Engineer Academy – the Future for MedTech Industries in Asia. The talk will end with an example of the most successful medical devices- the coronary stent as an example to demonstrate the importance of clinician and engineer partnership for a successful enterprise in medical technology.

Key Words: MedTech, Asia, Biomaterials, Tissue engineering, Regenerative medicine, 3D Printing, Creativity, Synapse firing, Clinician-engineer partnership, Entrepreneurship, Interdisciplinary, Successful enterprise

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Implementation of AI in Healthcare: Challenges and the Road Ahead

Prof Wong Tien Yin

Tsinghua University

Artificial intelligence (AI) has vast potential to impact on healthcare and ophthalmology. New AI models, including deep learning (DL), large language models (LLM) and foundational models (FM), have been now developed in medicine and may be useful in various clinical applications (e.g., clinical management recommendations, writing clinical notes, medical student tests etc), offering substantial opportunities to change current models of care. However, actual adoption and implementation of AI has been slow in clinical settings. Computer scientists and engineers in both academia and industry struggle to implement their AI models for clinical adoption and use. The reason is that clinical integration, adoption and implementation is related to a complex interaction of not just technical factors (how accurate or advance or mature is the AI technology?) but a range of non-technical factors. For example, many AI models have been only tested in highly experimental "lab settings" and not validated in "real-world" clinical settings and in local patient populations and context, making physicians and policy makers hesitant to embrace AI safely. Non-technical factors (e.g., patient and physician acceptance, clinical workflow process change, government funding and reimbursement) also impede the adoption and scaling of AI in healthcare. Understanding implementation science is critical for physicians, scientists, policy makers and healthcare leaders to allow AI to truly transform medicine and healthcare.

Methods for Evaluating the Accuracy of Artificial intelligence-based Medical Devices without a Gold Standard

Xiahua Zhou

Big Data Expert, Sch Pub Health, Peking University

Software as a Medical Device (SaMD) is proposed by the International Medical Device Regulators Forum (IMDRF) as "software intended to be used for one or more medical purposes that performs these purposes without being part of a hardware medical device."

The rapid development of artificial intelligence (AI)- and machine learning (ML)-based technologies in healthcare has intensified the derivation of SaMD. While these technologies demonstrate unprecedented capabilities in analyzing vast amounts of medical data, how to evaluate the performance of SaMD is facing big challenges. One of the main challenges is the frequent absence of a gold standard for performance evaluation of SaMD.

In this talk, I discuss various measures that can be used in the evaluation of SaMD and statistical methods for estimating those measures, particularly in the absence of a perfect gold standard.

Resolution, Reconstruction and Regulation of Tissue Fibrosis

Yanan Du
School of Medicine, Tsinghua University

A variety of diseases in multiple organ systems (e.g., liver, heart, lung, skin) are associated with fibrotic lesions. Fibrotic diseases have become one of the major health burdens in industrialized countries worldwide, directly or indirectly causing over 50% of deaths. Currently, there is a lack of effective treatments for tissue fibrosis or cirrhosis. Our team reported a novel pathological mechanism by which hepatic sinusoidal capillarization can promote liver fibrosis through "paratensile signaling" mediated by collagen fibers (Nature Materials, 2017), and further discovered that "paratensile signaling" can serve as a universal pathological mechanism for cell mechanical communication during the progression of various tissue fibrotic diseases (PNAS, 2020; Trends in Biology, 2022), expanding the cell communication scheme based on biochemical "paracrine signaling". We have also explored the mechanism by which "paratensile signaling" drive the formation of liver lobule structure and "pseudo-lobules" in liver fibrosis by regulating the directional migration of hepatic stellate cells (Nature BME, accepted). Meanwhile, we discovered that "advanced glycation end products" (AGE) cross-linking occurs in the collagen fibers of cirrhotic tissues, as well as the mechanism by which AGE cross-linking alters the mechanical properties of collagen fibers and promotes the occurrence of fibrotic diseases (Nature BME, 2023). These studies have inspired precise intervention and regulation therapies targeting "vascularization" and "extracellular matrix" within the pathological microenvironment of tissue fibrosis, providing new theories and strategies for conquering intractable fibrotic diseases such as liver cirrhosis.

Symposia 2
3D-printing Biomaterials

3D Printing Construction and Application Research of Anti-Inflammatory Bioresorbable Airway Stent

Chuhan Zhang [a, 1], Xiumei Mo [a,c *], Feng Hu [b, *],Binbin Sun [a, *]

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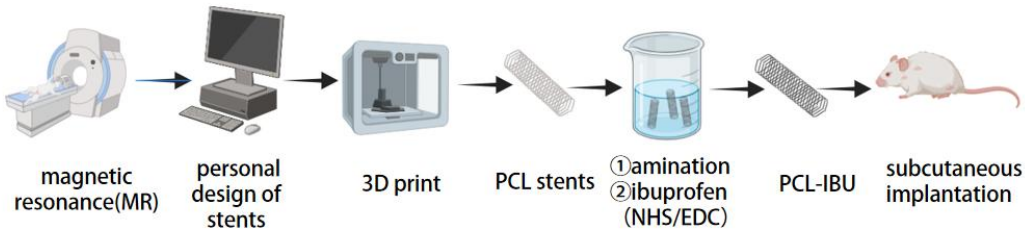
Central airway obstruction (CAO) As a common clinical critical illness, its treatment faces important challenges. Although surgical reconstruction is still the preferred method, some patients cannot tolerate surgical intervention due to systemic status or anatomical limitations. For such patients, airway stent implantation has become a key alternative therapy.

In this study, the biodegradable material of Polycaprolactone (PCL) was selected to fabricate a functionalized airway stent through 3D printing and surface modification technology. A three-dimensional finite element model was constructed using COMSOL Multiphysics 6.0 for mechanical analysis of the stent, while fused deposition modeling (FDM) combined with a rotating receiving platform achieved personalized customization of PCL stents. Furthermore, polyethyleneimine (PEI) surface cross-linking was employed to create an aminated PCL stent, with covalent bonding used to graft the anti-inflammatory drug ibuprofen onto the stent surface. Mechanical testing demonstrated that the 3D-printed PCL-IBU stents exhibited superior radial strength and compression resistance. In vitro experiments confirmed the excellent cytocompatibility of the stents. The functionalized stents downregulating the expression of pro-inflammatory genes while upregulating anti-inflammatory markers . Additionally, they significantly suppressed production of reactive oxygen species (ROS) and nitric oxide (NO) in macrophages.In rat subcutaneous implantation experiments, compared to unmodified PCL stents, the PCL-IBU stents markedly reduced inflammatory responses.

This study highlights the potential of 3D-printed personalized PCL-IBU stents to address clinical limitations of conventional stents, including the requirement for secondary removal surgery, inadequate anatomical adaptability, and severe postoperative inflammation, thereby offering a promising therapeutic strategy for repairing airway stenosis.



Key words: Biodegradable coronary stents；3D printing；Personalized；ibuprofen；Anti-inflammatory；Tissue engineering

Acknowledgments

This research was supported by the Medical-Engineering Interdisciplinary

Collaborative Project between Shanghai Tongren Hospital and Donghua University

3D printed ALA-Eth/MgO/PLCL/PLGA composite scaffold by low-temperature deposition modeling for innervated bone regeneration

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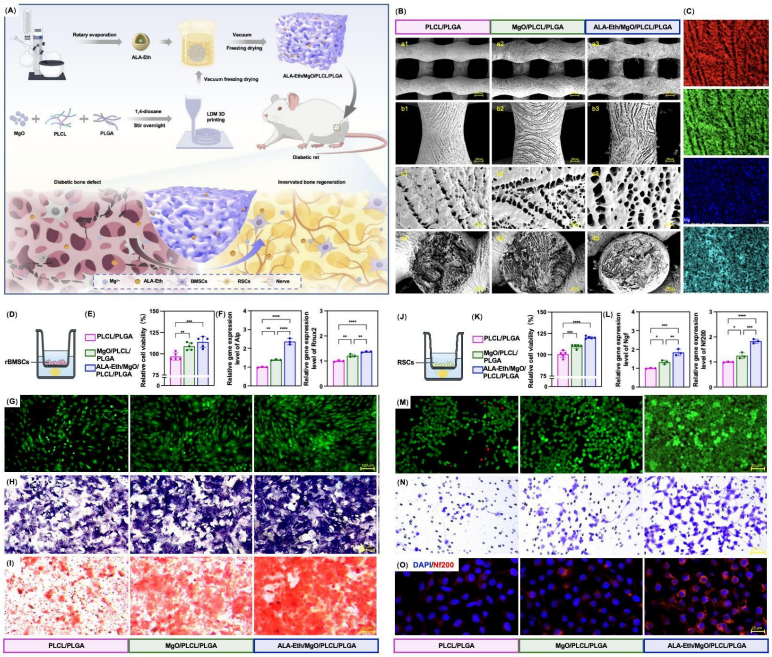
The rising global prevalence of diabetes mellitus (DM) has positioned diabetic bone defects as a pressing clinical challenge requiring urgent attention [1]. A major complicating factor is diabetic peripheral neuropathy (DPN), which affects up to 50% of DM patients and exacerbates the pathological microenvironment at bone lesion sites, severely impairing regenerative capacity [2]. While α-lipoic acid (ALA), an established neuropathy treatment, has demonstrated neuroprotective and pro-regenerative potential, its targeted delivery remains a hurdle. To address this, we developed a low-temperature deposition modeling (LDM) 3D-printed scaffold using a hybrid ink composed of magnesium oxide (MgO) and poly(lactic-co-glycolic acid) (PLGA)/poly(lactide-co-caprolactone) (PLCL) for sustained release of ALA-loaded ethosomes (ALA-Eth). In vitro cell experiments showed that the hierarchical porous scaffold achieved extended bioavailability, remarkable cellular function of the rat Schwann cells (RSCs) and superior bone-forming ability of the rat bone marrow mesenchymal stem cells (rBMSCs) under high-glucose conditions. Collectively, this study introduces an innovative LDM-fabricated scaffold that synergistically promotes neuroregeneration and osteogenesis, offering a promising therapeutic strategy for diabetic bone repair.



Key Words: diabetic bone defect, 3D bioprinting, α-lipoic acid, innervated bone regeneration

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Integrating Bioprinting with Organoids for Biomedical Applications

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Additive manufacturing (AM, popularly known as "3D printing") emerged in the 1980s and has made profound impacts in our society. The biomedical industry has benefitted hugely by employing AM technologies in fabricating various biomedical products (simple or complex), which can be in large quantities and are also of consistent quality [1]. Over the past decade, AM has evolved from 3D printing to 4D printing to current 5D printing, which enables fabrication of dynamic, self-adapting and interactive products for applications in highly demanding situations in areas including biomedical [2]. Bioprinting first appeared in 1988 when Klebe used a standard Hewlett-Packard inkjet printer to deposit cells for constructing synthetic tissues in 3D. 3D/4D/5D printing and bioprinting are powerful manufacturing platforms for making various complex and personalized medical products, including those for regenerating complex body tissues such as uterine tissue [3]. Over the years, for making cell-laden objects using different technologies including bioprinting, the cellular usage has progressed from cells to spheroids to organoids. Organoids are multicellular systems that self-organize into structures resembling an organ or organ region. Compared to individual, non-organized cells or spheroids, organoids provide the particular advantages of capturing the cell type diversity, gene and protein expression and microscale cytoarchitecture shown in native tissue and hence employing organoids for producing cell-embedded systems enables creation of biomimicking structures (microtissue, microtumor, etc.) that are much closer to those of native tissues, which will lead to much better research or clinical outcomes. A major disadvantage for organoids is that their self-organization ability is limited to a length scale in the order of hundreds of micrometres, thereby restricting their ability to self-organize into larger tissue structures. The great power of bioprinting can thus highly assist, with the use of organoids, the biofabrication of large-size tissue-mimicking structures and models. As now is still the early stage of integrating bioprinting with organoids, there are many challenges in nearly every aspect of organoids bioprinting, including ink materials, availability (particularly tumor organoids) and technology for organoids, bioink formulation, bioprinting technology, multi-bioink printing, etc. For example, among major bioprinting technologies, i.e., inkjet-based bioprinting, light-assisted bioprinting and extrusion-based bioprinting, extrusion-based bioprinting is most often used but their printing resolutions are limited. Technological innovations (e.g., Kenzan bioprinting) are thus needed for organoids bioprinting. Currently, for most organoid models, a model uses a single type of organoids and hence represent a single tissue region of the body. New strategies/technologies are needed for multi-bioink organoid printing that will re-create complex tissue or organ structures/models. Applications of bioprinted organoids structures/models range from developmental biology, cancer research, drug discovery, to regenerative medicine. This keynote talk will provide an overview of organoids bioprinting, look into challenges and highlight some possible solutions for organoids bioprinting, as well as introducing some of our work in organoids bioprinting.

Keywords: organoid, bioprinting, bioink, cancer research, drug screening, tissue engineering

Acknowledgements: Our research has been supported by research grants from Hong Kong's Research Grants Council (RGC) and China's National Natural Science Foundation (NSFC) and by HKU.

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3D printed high-strength natural polymer hydrogel bilayer scaffold for cornea regeneration

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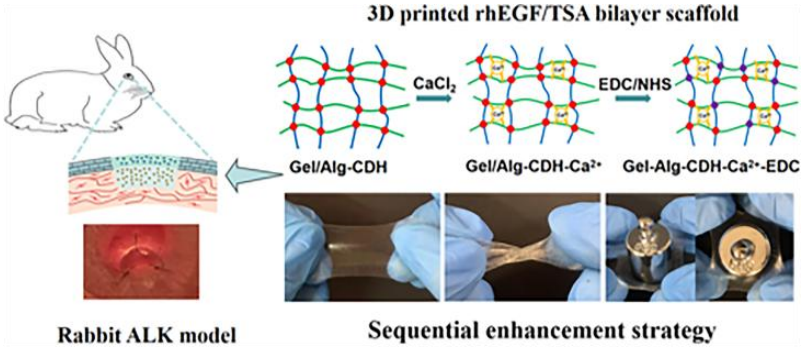
Introduction: Currecntly, the emerging 3D printing technology offers a new concept for the design of biomimetic cornea scaffolds that structurally mimic the complex multilayer structure of natural cornea and allows the precise introduction of desired cells/activators in different geometric layers. However, the preparation of 3D printed natural polymer hydrogel scaffolds with excellent mechanical properties similar to that of natural cornea tissues presents significant challenges.

Research design: We developed a hydrogen-bonding enhanced gelatin/carbohydrazide modified alginate extrusion printing ink (Gel/Alg-CDH) and a matching sequential strengthening strategy to improve the mechanical property. In addition, we prepared rhEGF/Trichostatin A-loaded bilayer Gel-Alg-CDH-Ca^{2+}-EDC hydrogel scaffolds to mimic the epithelium-stroma structure of the natural cornea.

Main results: The Gel-Alg-CDH-Ca^{2+}-EDC hydrogels exhibited a high transparency, physiological swelling stability and rapid enzymatic degradability, as well as suturability. In the rabbit ALK model, the rhEGF/TSA-loaded hydrogel scaffold resulted in the formation of integrated epithelium-stroma structure resembling normal corneal tissue.

Discussion: Development of Gel/Alg-CDH inks and the sequential strengthening strategy provides an ideal option for bioprinting high-strength and tough corneal scaffolds, and this idea can be extended to construct a variety of high strengh wholly natural polymer hydrogels due to its simplicity and versatility.

Conclusion: This bioactive bilayer hydrogel scaffold considerably promotes regeneration of corneal epithelium and stroma, and inhibits cornea scarring in rabbit cornea keratoplasty.



Key Words: 3D printing, high-strength hydrogel, bilayer scaffold, cornea regeneration

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Symposia 3
Advanced Biomaterials

Design And Fabrication Of Biodegradable Mg Alloy With Superior Strength And Ductility For Bone Implants

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Mg alloys possess great potentials in the biomedical fields due to their biodegradation, medium strength and good biocompatibility. However, there is always a concomitant decrease in ductility during strengthening in Mg alloys, resulting in an undesirable strength-ductility trade-off. Therefore, the development of Mg alloys with high strength-ductility synergy is highly demanded for their wider applications. In this study, the as-extruded biodegradable Mg-Nd-Zn-Zr (JDBM) alloy rod was subjected to single-pass drawing over a range of temperature 200 ~ 600 °C to enhance the properties. After drawing, a more homogeneous and refined microstructure developed because of dynamic recrystallization (DRX) and dynamic precipitation (DP). With the increase of drawing temperature, grain sizes increased first and then decreased due to the competition of grain nucleation and growth, while the sizes of the secondary phase particles varied in the same way. And a nearly basal texture evolved from a rare earth texture of the as-extruded sample. The yield strength of the as-drawn samples increased by ~2.2 times with a sacrifice of elongation to fracture at different level. The high yield strength mainly originated from grain boundary and dislocation strengthening. An optimal combination of high yield strength (~301 MPa) and good ductility (elongation to fracture of ~19% and improved strain hardening capacity) was obtained after drawing at 500 °C. The yield strength enhancement was mainly derived from texture and dislocation strengthening. Grain and secondary phase particle refinement, large volume fraction of low angle grain boundaries and reduced geometrically necessary dislocations are considered to be beneficial to the good ductility. In addition, a novel method has been proposed to fabricate materials with superior strength-ductility synergy by deformation with large strain at high temperatures to activate severe DP [1]. JDBM magnesium alloy bone screws prepared by the above process have successfully carried out 176 multi-center human clinical trials (Fig.1).

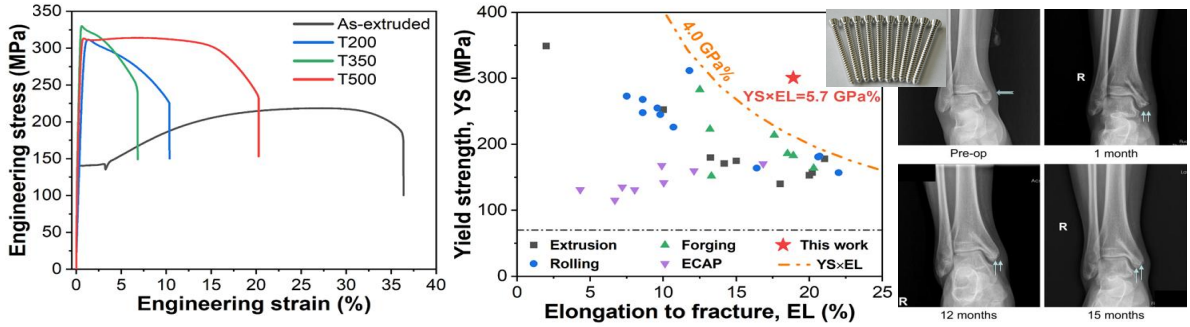

Fig. 1 Mechanical properties of JDBM rods for bone screws and their clinical trial

Key Words: Biodegradable Mg alloy, Bone implants, Hot drawing, Strength and ductility synergy

Acknowledgements: This work was supported by The National Key Research and Development Program of China (No.2021YFC2400701)

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Keratins as a Sustainable Material for Biomedical Applications

Kee Woei Ng[1,2,3]

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The demand for sustainable biomaterials is expected to intensify. Nature derived biomaterials are not new and have been widely discussed in the literature. Keratins are a more recent example and are one of the very few human-derived materials that are readily available in abundance. Other than human hair, animal keratins are also easily obtained from farming waste streams such as feathers and wool. Keratins are unique because they contain high proportions of functional groups, especially thiols, to support chemical interactions. Together with their inherent propensity to self-assemble into organized structures, keratins have been demonstrated to be easily processable into a variety of physical formats. These keratin formats have been found to be biocompatible and capable of inducing positive cell responses to support the regeneration of different tissues.

Our group has developed a cryogelation technique which allowed 3D keratin-based hydrogels with tunable physical properties and microarchitectures to be produced. Strain-stiffening behavior can also be induced by crosslinking keratins and dopamine through a similar cryogelation process. We further made use of thiolate interaction with cations to provide the possibility of a rapid gelling system for bioink development. This cationic induced gelation method allowed the production of a gradient hydrogel through a single-step fabrication process. By using silver ions as the cationic crosslinker, a gradient hydrogel that releases silver ions as an antimicrobial agent, as the gel degrades, is produced. More recently, we adopted the technique of Interfacial Polyelectrolyte Complexation (IPC) to produce keratin-based fibers. Keratins were pH adjusted to produce polycationic or polyanionic solutions and partnered together or with established polycations such as chitosan and drawn to produce the micrometer-sized fibers. These fibers exhibited good mechanical properties that were comparable to commercial suture materials. An *in vivo* study found these fibers to function well as a suture for closing full-thickness cutaneous wounds in mice, resulting in minimal host tissue response over a 3-week period. Our work has demonstrated that keratin-based templates are versatile, functional and could provide meaningful outcomes in tissue engineering applications.

Key Words: biomaterial, keratin, tissue engineering, sustainable

Acknowledgements: This research is partially funded by the Indonesian Endowment Fund for Education (LPDP) on behalf of the Indonesian Ministry of Education, Culture, Research, and Technology and managed under the INSPIRASI Program (Grant No 6636/E3/KL.02.02/2023).

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Effect of lavender essential oil on properties of chitosan-based films

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Chitosan-lavender essential oil composite films were prepared with chitosan (CS) and lavender essential oil (LEO) by a casting-evaporation-alkali leaching method. The microstructure of the films was characterized by scanning electron microscope (SEM) and Fourier transform infrared spectroscopy (FTIR).The influences of LEO concentration (0%, 2%, 4%, 6%, 8% and 10%) on the thickness, mechanical properties, volatile content, water contact angle, water vapour permeability, total soluble matter content of films were investigated. The partial functional group locations in the CS matrix were occupied by LEO ingredients, leading to a decrease in free hydrogen groups forming hydrophilic bonds with water. The water contact angle increased in line with the LEO concentration, and LEO incorporation caused an increase of chitosan-acetate content, furthermore, leading to a higher total soluble matter content of the films. The film thickness ranged from 20.60 ± 0.34 to 23.35 ± 0.65 μm. When the LEO concentration was 8 %, the tensile strength and percentage elongation at break reached maximum values of 123.44 ± 0.33 MPa and 3.74 ± 0.02%, respectively. The volatile content was reduced by the addition of LEO. The CS-LEO (2%) film exhibited the best water vapour barrier properties.

Keywords: chitosan; lavender essential oil; film; mechanical properties; physical properties

Table captions:
Tab.1 Essential oil composition of Lavender
Figure captions:
Fig.1 Chitosan films containing LEO at level to 0, 2, 4, 6,8 and 10% (v/v).
Fig.2 SEM photographs of CS-based films with different LEO concentration.
Fig. 3. FTIR spectra of films: A, CS film; B, CS-LEO (2%) film; C, CS-LEO (4%)film; D, CS-LEO (6%) film; E, CS-LEO (8%) film; F, CS-LEO (10%) film; G, LEO.
Fig. 4. Influence of LEO concentration on thickness of CS-based films. Different letters indicate significantly difference ($p<0.05$) when analyzed by Duncan’s New Multiple Range Test.
Fig. 5. Influence of LEO concentrations on TS and E% of CS-based films. Different letters indicate significantly difference ($p<0.05$) when analyzed by Duncan’s New Multiple Range Test.
Fig. 6. Influence of LEO concentration on volatile content of CS-based films. Different letters indicate significantly difference ($p<0.05$) when analyzed by Duncan’s New Multiple Range Test.
Fig. 7. WCA values of CS film and films containting LEO at level of 2, 4, 6, 8 and 10%, respectively. Different letters indicate significantly difference ($p<0.05$) when analyzed by Duncan’s New Multiple Range Test.
Fig.8. Influence of LEO concentration on WVP of CS-based films. Different letters indicate significantly difference ($p<0.05$) when analyzed by Duncan’s New Multiple Range Test.
Fig. 9. Influence of LEO concentration on TSMC of CS-based films. Different letters indicate significantly difference ($p<0.05$) when analyzed by Duncan’s New Multiple Range Test.

Tab 1

No	Compound	% of the total peak area
6.317	3-Methyl-2-butena	0.01
6.681	n-Butyl acetate	0.03
6.919	n-Hexyl Ether	0.05
7.470	3-Hexenol(Z)-3-hexene Blatteralcohol	0.03
7.681	Hexyl formate	0.08
8.518	Butyl Propionate	0.01
9.221	α-thujene	0.08
9.522	α-pinene	0.16
10.093	camphene	0.17
10.714	1-Octen-3-ol	0.26
10.929	3-octanone	1.33
10.988	β-pine	0.07
11.062	β-Myrcene	0.55
11.156	n-butyl butyrate	0.12
11.277	3-Octanol	0.23
11.496	cis-3-hexenyl acetate	0.01
11.738	Hexyl acetate	0.61
11.883	α-Phellandrene	0.02
11.985	δ-carene	0.13
12.321	1-methyl-2-propan-2-ylbenzene	0.45
12.809	cis-Ocimene	3.83
12.907	sabinene	0.20
12.985	cineole	1.39
13.243	β-trans-ocimene	1.80
13.849	γ-Terpinene	0.05
14.376	cis-epoxydihydrolinalool	0.20
15.021	α-Terpinene	0.13
15.068	rosefuran	0.06
16.014	Linalool	31.23
16.120	cis-hydrated sabinene	0.02
16.292	3-octyl acetate	0.19
16.776	Ocimene	0.06
16.936	1,2,3,4-Tetrahydrophenl	0.06
17.265	cis-epoxy Ocimene	0.03
18.101	camphor	0.26

18.453	Lavandulol	0.77
18.895	galbanolen	0.03
19.195	Borneol	0.79
19.371	isopinocamphone	0.10
19.555	Alpha-Terpineol	3.91
19.829	cryptone	0.32
20.380	octyl acetate	0.03
20.642	2,6-Dimethyl-3,5,7-octatriene-2-ol	0.07
21.455	Nerol	0.27
21.619	Hexyl 2-methylbutanoate	0.03
21.693	bornyl formate	0.07
22.768	Linalyl acetate	34.29
22.924	benzyl alcohol	0.01
23.112	piperitone	0.02
23.983	Lavandulyl acetate	4.03
24.108	Phellandral	0.03
24.284	bornyl acetate	0.27
24.558	Cumic alcohol	0.07
25.543	piperitenone	0.03
26.219	ethyl tiglate	0.04
27.333	Benzyl butyrate	0.01
27.415	Terpinyl acetate	0.01
27.915	Neryl Acetate	0.50
29.197	Geranyl acetate	0.76
29.514	Copaene	0.02
29.678	hexyl hexanoate	0.08
30.072	bergapten	0.17
32.359	safranal	0.02
32.656	α-santalene	0.45
33.582	α-bergapten	0.15
34.067	Coumarin	0.03
34.161	sesquiphellandrene	0.08
34.532	Aromadendrene	0.04
34.790	Norbornene	0.02
37.690	myrcene	0.61
38.733	Bicyclic-germacrene	0.02
39.070	(E,E)-α-Farnesene	0.01
39.472	β-Bisabolene	0.04
40.027	γ-Cadinene	0.10
45.190	(-)-β-caryophyllene	0.51

49.134	(+)-Epi-Bicyclic-sesquiphellandrene	0.07

Figure 1

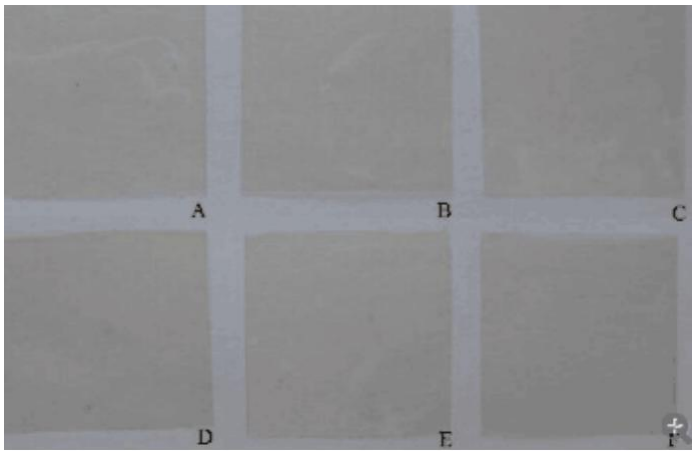
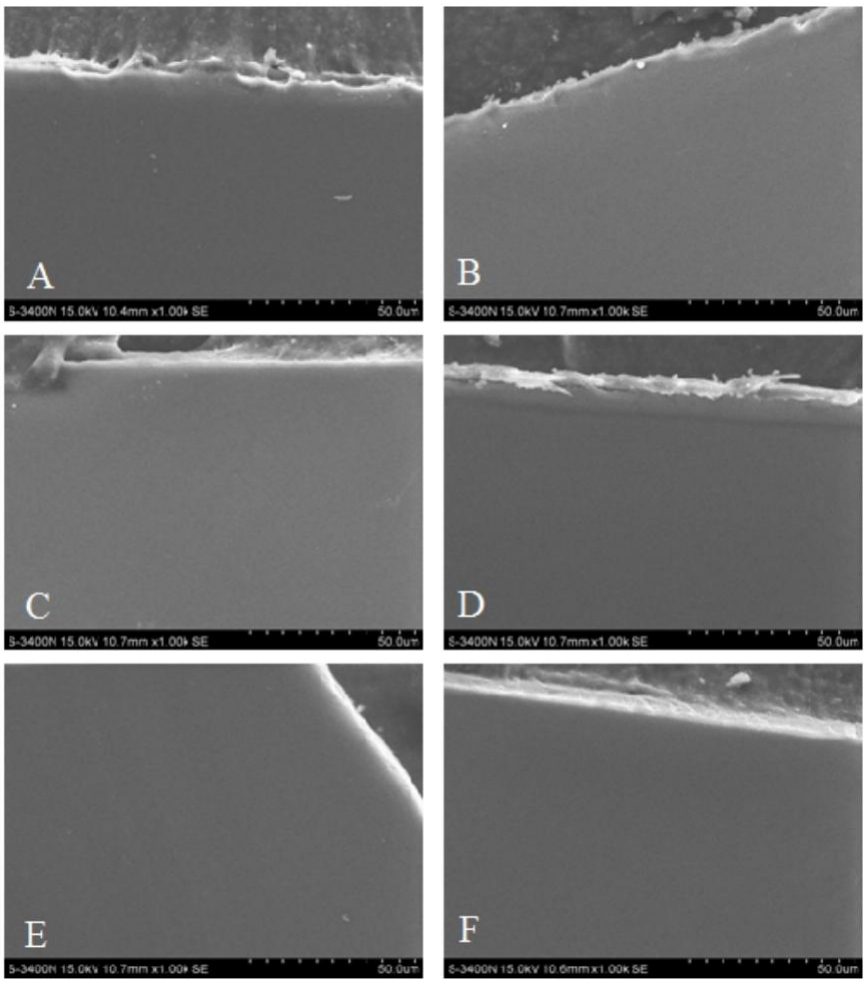


Figure 2



A, CS film; B, CS-LEO (2%) film; C, CS-LEO (4%) film; D, CS-LEO (6%) film; E, CS-LEO (8%) film; F, CS-LEO (10%) film.

Figure 3

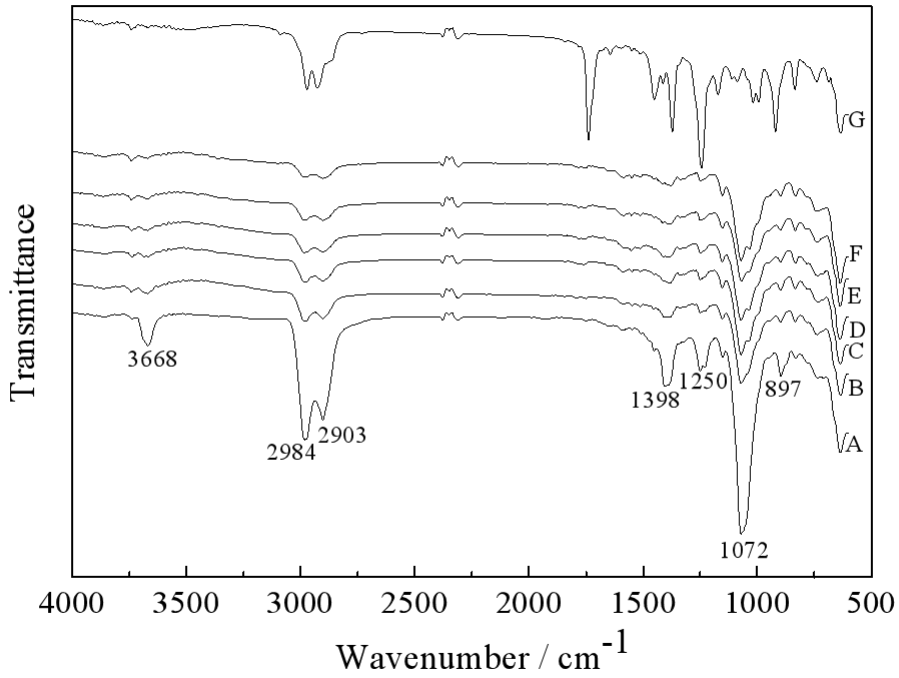


Figure 4

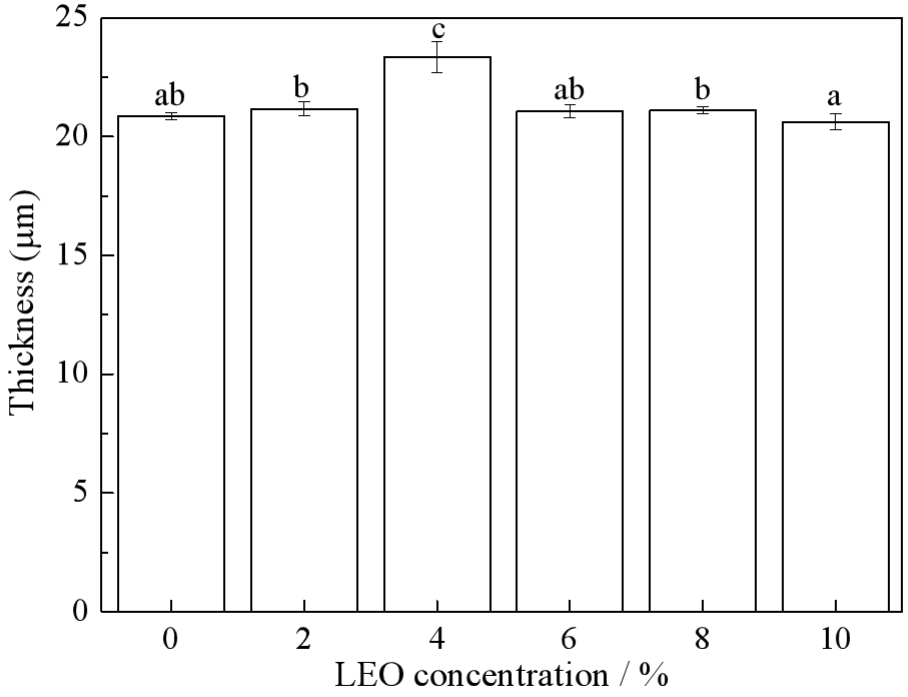


Figure 5

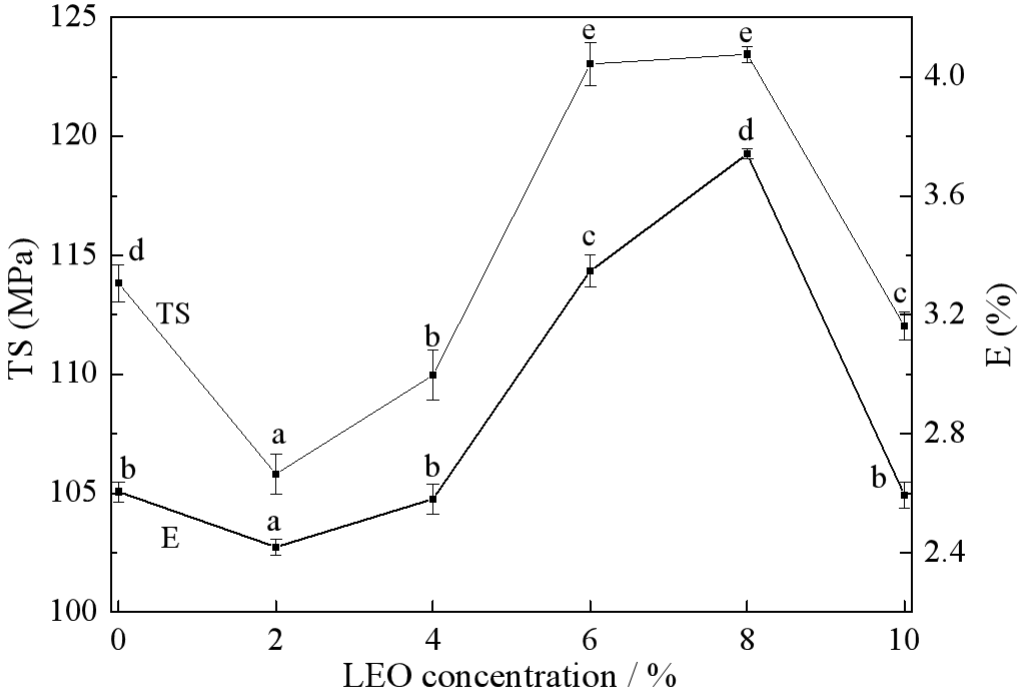
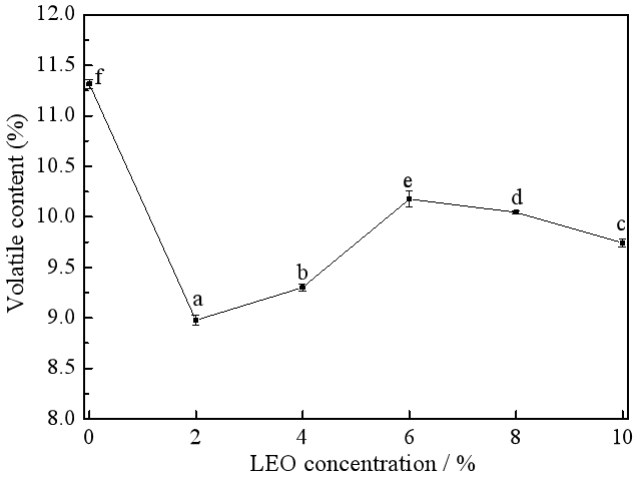


Figure 6



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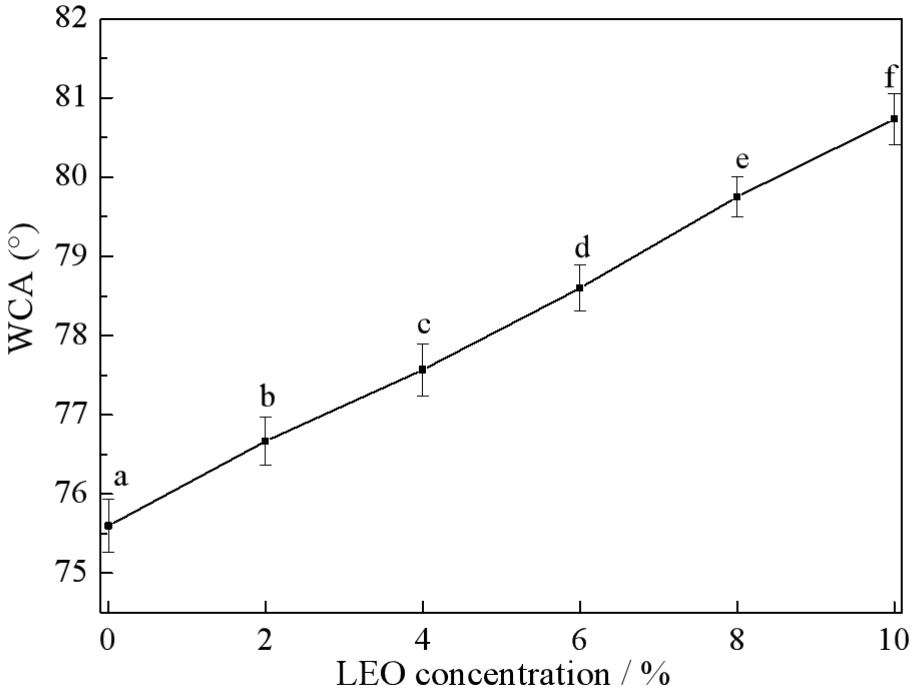


Figure 8

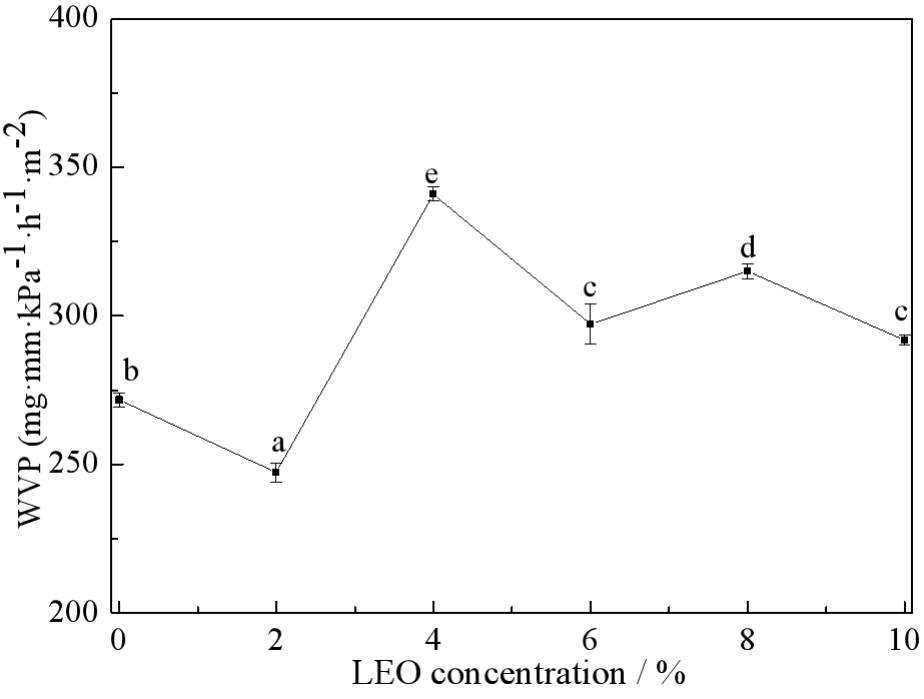
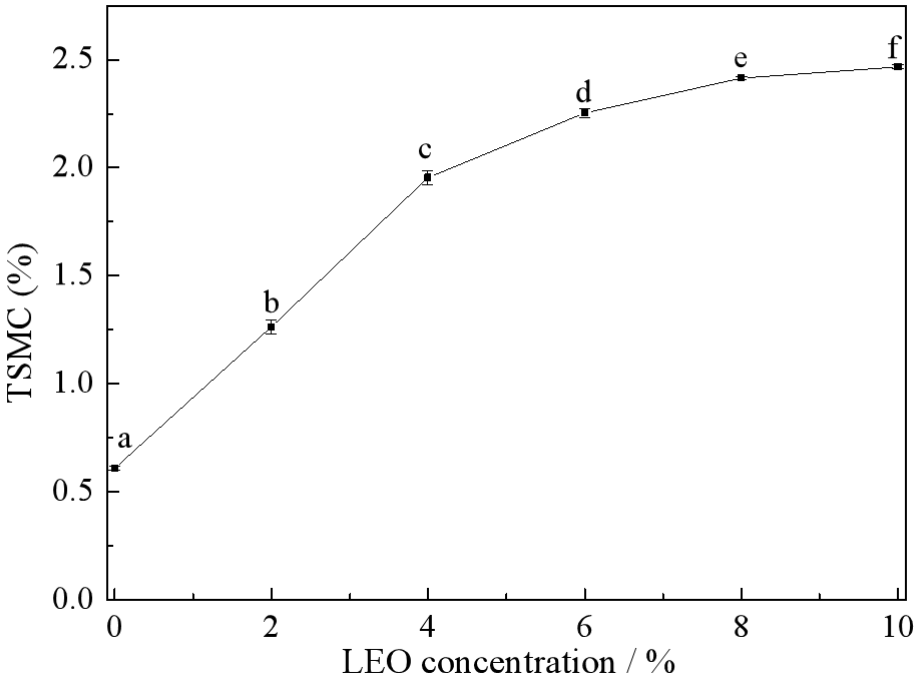


Figure 9



Acknowledgments

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Innovation and Translation for Bioactive Bone Grafts in China

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Abstract

The current lecture includes the following parts: 1) The structural characteristics of human bone tissues;2) R & D of a new generation of bioactive bone grafts; 3) Translation of Bioactive Bone Grafts in the Chinese market; 4) Facilities and conditions for translation available at HUST.

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3D printed smart piezoelectric scaffolds for spatial-temporal control for bone regeneration

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Bone regeneration constitutes a precisely orchestrated process governed by spatiotemporal coordination of biochemical signaling, bioelectrical cues, and mechano transduction pathways [1.2]. We reported a breakthrough in 3D printing, biodegradability, and ultrasound-triggered spatiotemporal control and allows precise, on-demand stimulation. Gradient Barium titanate (BTO) distribution (5% vs. 10%) enables spatial control of osteogenesis. For the first time we link piezoelectric scaffolds to CD31+/VEGF+ H-type vessels, crucial for coupling angiogenesis and osteogenesis. Spatial control is achieved by guiding bone formation within 3D printed specific regions of calvarial defects in rats. Temporal control is regulated through ultrasound stimulation, which modulates distinct stages of bone healing. However, developing a smart scaffold that is bioactive and piezoelectric and suitable for 3D printing is a major challenge, especially in terms of uniform dispersion and rheological properties. This study found a solution to implement a 3D printed composite scaffold consisting of PBT (BTO packet of polydopamine dispersed over the TCP surface) and PCL. The scaffold promoted the anti-inflammatory bone immune microenvironment and increased the percentage of M2 macrophages and osteoblasts. In summary, the breakthrough in the design of the composite piezoelectric scaffold stimulated by ultrasound can activate the surrounding cells to release growth factors such as BMP2 and VEGF, which has the function of bone immune regulation mediated by macrophages. This work establishes a new paradigm for intelligent bone scaffolds that synchronize electromechanical stimulation with immunomodulation for enhanced tissue regeneration.

Key Words: Bone regeneration, Osteogenesis, Piezoelectric Materials,3D Printing, Macrophage Regulation, Ultrasound Stimulation

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Scientific Publishing: An *Advanced* Perspective

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A highly competitive research environment with increasingly limited research funding has created a "Publish or Perish" attitude among scientists who are judged on both the quantity and the quality of their research articles. This presentation provides a brief overview of recent development of scientific publishing, and how manuscripts are handled by in-house editorial staff (including prescreening, finding referees and making decision on referees' reports). Tips will be presented on how to select an appropriate journal for your paper, what aspects of preparation and presentation to focus on from an editor's and referee's perspective, and how to increase the visibility of your paper after publication during the manuscript writing and preparation.

Key Words: Scientific Publishing, Advanced, Peer Review, Biomaterials

Biomimetic elastomers, 3D printing and their biomedical applications

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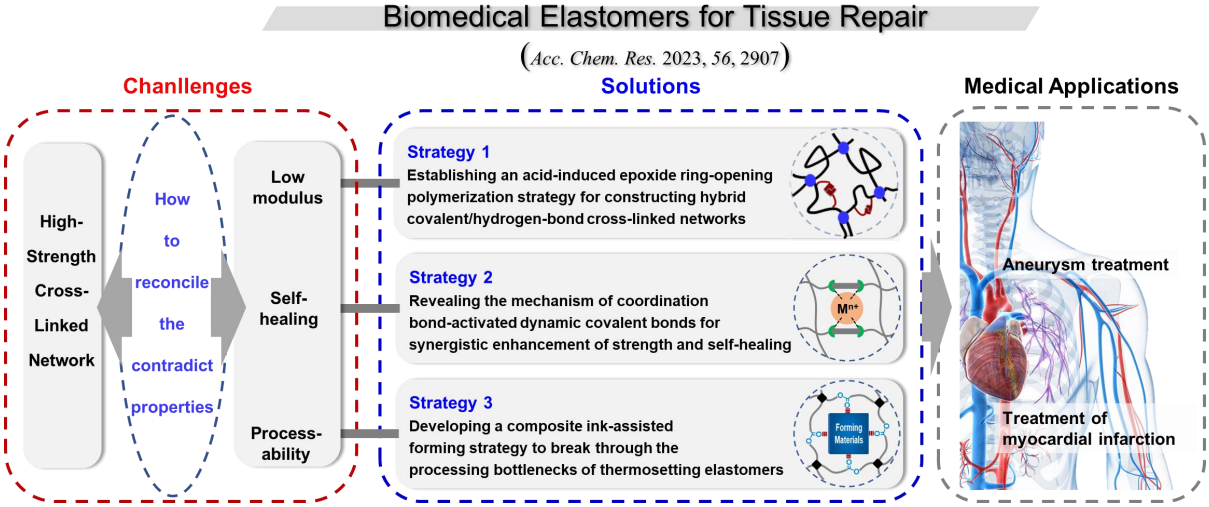
Owing to their potential of biomimetic mechanical properties, elastomers have been extensively used, and become more and more important in biomedical fields such as medical implants, regenerative medicine, and bioelectronics. In addition to further enhance the common properties of elastomers, it is highly desired to endow elastomers with functionalities such as reprocessability, biomimetic mechanical properties, self-healing ability, bioactivity, and electrical conductivity, which will significantly broaden their applications. The covalent or non-covalent cross-linked structure is the essential factor for the elasticity of elastomers. Traditional elastomers usually compose of single type of cross-linked molecular network, which is difficult to modulate the properties and introduce functionalities. Inspired by the simultaneous existence of multiple cross-linked structures in proteins, we have employed hybrid cross-linking strategy to construct elastomers. Various noncovalent interactions (e.g., hydrogen bonds, cation-π interaction[1] and coordination bonds) and dynamic covalent bonds (e.g. oxime-urethane bonds[2], and urea bonds, disulfide bonds) have been integrated in elastomers. Accordingly, the properties and functionalities of elastomers can be tuned by regulating the types, ratios, and distributions of cross-links. The hybrid cross-linking strategy provides a versatile and effective way to construct diverse functional elastomers for broad applications. In this talk, we present our recent progress on functional elastomers constructed by hybrid cross-linking strategy, including their design, preparation, properties, 3D printed devices and their diverse biomedical applications including bioelectronics, tissue regeneration and treatment of cardiovascular diseases.[3]



Key Words: Elastomer, self-healing, hybrid cross-linking, polyurethane, 3D printing

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Light/ultrasound-driven organic-inorganic hybrid nanomaterials

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Cancers, pathogenic bacteria, and viruses bring severe threats to human health. Novel biomaterials and related therapies have been urgently explored to improve therapeutic efficacy and alleviate side effects. The organic-inorganic hybrid materials are capable of the advantages of both organic and inorganic materials while avoiding their drawbacks, which attract great attention. We have developed the following three strategies in this field. First, we prepared some polymer-coated inorganic semiconductor nanoagents (such as $W_{18}O_{49}$) that could convert near-infrared light into heat for photothermal ablation of tumors. The inorganic photothermal agents were combined with thermosensitive hydrogel and chemo-drug (G-CuS-DOX) to achieve multifunctional therapy[1]. Highly sensitive photosensitizers interacted with metal ions to result in phototoxicity inhibition and photothermal activation. Second, we developed various metal-organic frameworks (such as Pd-hemoporfin[2]), which reversed tumor microenvironments and were activated by tissue-penetrating ultrasound and X-ray. Third, we developed some nanofiber membranes for the rapid destruction of bacteria and viruses upon irradiation of an infrared baking lamp. We have further developed photo-responsive fibers to reduce bacterial infections and promote wound healing[3]. Therefore, these hybrid materials have played a vital role in fighting against these diseases.

Key Words: hybrid nanomaterials; tumor therapy, sterilization; wound healing

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Symposia 4
Bio-inspired drug delivery systems

Development of microneedle devices with anisotropic porous structure for biomedical application

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Introduction: Porous microneedle (MN) devices allow optimal performance in drug delivery and body fluid sampling. Unfortunately, the available porous MNs contain randomly interconnected pores, and existing MN fabrication methods cannot control the pore diameter and pore running direction.
Research design: This work used a freeze-casting technique to control these parameters in porous MNs inspired by the anisotropic porous structure of the wood xylem.
Main results and discussion: This microstructure allows liquid absorption from tips to base within seconds as a tear sampling tool to monitor the tear biomarkers, which has been confirmed in rat dry eye disease and diabetes models. The anisotropic porous MNs also supports the active loading of various drugs including γδ T cells from base to tips without the need for specialized equipment. γδ T cells delivered by the MNs can against tumors in both xenograft melanoma mouse model and pleural mesothelioma mouse model, providing an alternative way to deliver adoptive cells.
Conclusion: These findings demonstrated that MNs with anisotropic porous structure are versatile devices as noninvasive tear sampling tool as well as equipment-free drug loading and delivery platform.

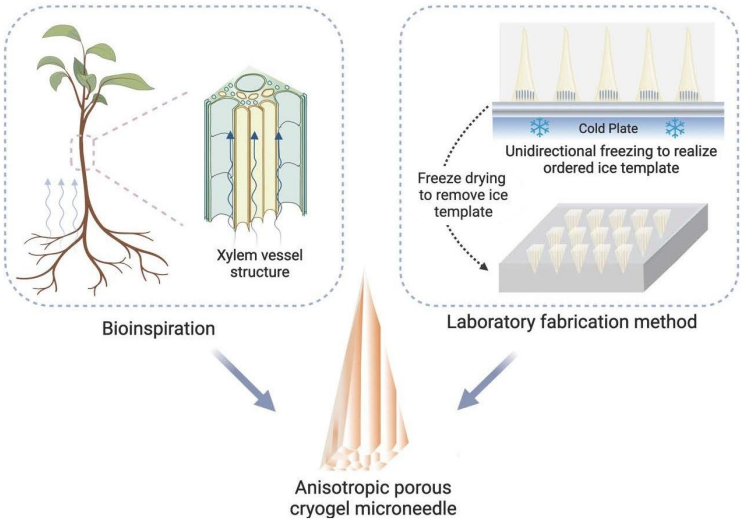

Figure 1. Schematic illustration of microneedles with an anisotropic porous structure. The wood xylem-like microstructure was developed by the unidirectional freeze casting technique. The potential applications of this device include tear sampling and adoptive cell delivery.

Key Words: Biomimicry, microneedles, anisotropic porous structure, drug delivery, diagnosis

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Bio-Responsive Supramolecular Prodrug Hydrogel for Precise Cancer Immunotherapy

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Cancer immunotherapy agents, especially immunocheckpoint inhibitors, cytokines and sting agonists have shown good therapeutic potential in clinical practice. However, traditional systemic administration often leads to the non-specific binding of immunotherapeutic agents in normal tissues, which results in serious immune related side effects. Moreover, due to immunosuppressive tumor microenvironment and insufficient infiltration of immune cells such as T cells into tumor tissue, the clinical response rate of immunotherapy is very low. Studies have shown that chemotherapy drugs can induce immunogenic cell death, and then enhance T cells, macrophages or dendritic cells and other immune cells to infiltrate into tumor tissue, thus providing the possibility of combination of chemotherapy and immunotherapy. In light of this, we prepared a series of bio-responsive supramolecular prodrug hydrogels with chemotherapeutic drugs, and used them as carrier to locally deliver immunotherapeutic agents to tumor site. The degradation of such hydrogel to tumor microenvironment stimulation (such as enzyme and GSH) can achieve "on-demand drug release", and then "re-edit" tumor microenvironment to combat cancer. In particular, according to the characteristics of different immunotherapy agents, we precisely designed the prodrug hydrogel system that matches its delivery needs. The combination of chemotherapy and immunotherapy can further improve the immunogenicity of tumor and the response of tumor to immunotherapeutic agents, and achieve collaborative precision treatment. This system can not only make tumor therapeutic drugs accumulate in tumor site and induce strong anti-tumor immune response, but also avoid the accumulation of immunotherapeutic agents in normal tissues, thus greatly reducing immune related side effects. In particular, the immunotherapeutic agents can not only take effect locally, but also induce a systemic anti-tumor immune response, thereby inhibiting tumor recurrence and metastasis.

Key Words: Peptide-drug conjugate, in-situ formed hydrogel, tumor microenvironment, cancer immunotherapy

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Delivery of Therapeutic Genome-Editing Biomacromolecues

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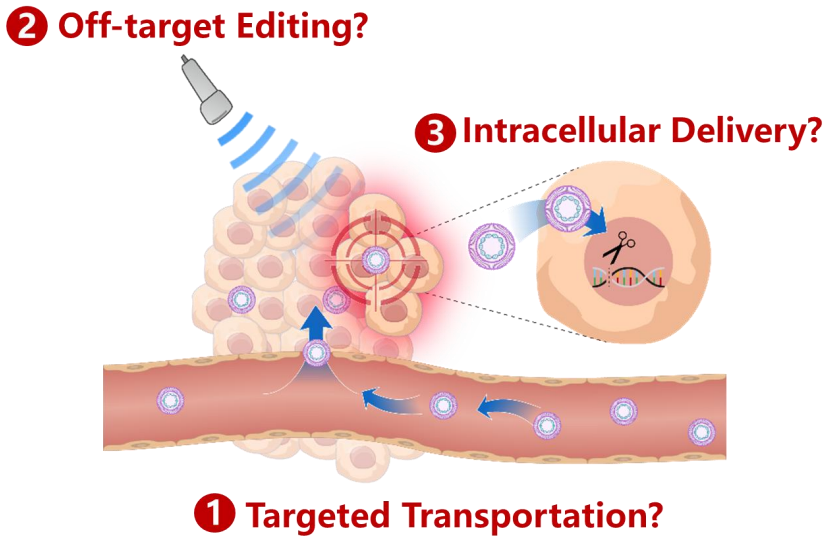
The clustered, regularly interspaced, short palindromic repeat (CRISPR)-associated nuclease 9 (CRISPR/Cas9) is emerging as a promising genome editing tool to treat diseases in a precise way, and now it has been applicable to a wide range of research in the areas of biology, genetics, and medicine. In vivo delivery of therapeutic genome-editing biomacromolecules provides a promising platform for the treatment of genetic disorders. In this talk, I will first discuss the barriers in the delivery process and the application of CRISPR/Cas9 system for the treatment of genetic disorders. Then, I will show several viral and non-viral systems for the targeted delivery of CRISPR/Cas9, and how we mitigate off-targets effects at the tissue level. Finally, I also highlight several representative types of non-viral vectors, including polymers and lipid nanoparticles for the intracellular delivery of CIRSPR/Cas9. The future prospects of delivery of CRISPR/Cas9 in treating genetic and other disorders will also be discussed.



Key Words: drug delivery, CRISPR-Cas9, bio-responsive genome editing, genetic disorders, non-viral delivery systems

Acknowledgements: This work was supported by Natural Science Foundation of China (NSFC) Distinguished Young Scholar Program (82425055).

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Symposia 5

Bioactive glasses and Glass-ceramics for HealthcareApplications

Self-setting polyphosphate coacervate composites for hard tissue repair

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Abstract:

Inorganic polyphosphate is a special linear biopolymer composed of total inorganic units—phosphoric acid/phosphate residues. Such compounds are naturally present in both human bodies and microbial systems, where they play the key roles in a variety of biological actions including biomineralization, blood coagulation and energy metabolism. Therefore, it is promising to establish the PolyP-based biomaterials for hard tissue regenerations which deeply demand the promotion on biomineralization and energy metabolism. Herein, we developed the self-setting composites (denoted as PolyPIS) based on a special viscous liquid—polyphosphate coacervate, a special condensate formed via the complex noncovalent interaction between polyphosphate and Ca^{2+}. We investigated the physical and chemical characteristics of PolyPIS, and particularly demonstrated their exceptional performance as the hard tissue repair agents. The self-setting nature, great adhesion to the tissues, biocompatibility, and ability to promote energy metabolism enable PolyPIS to perform very well in saving the dental pulp and repairing the bones, which are confirmed both in vitro and in vivo (Figure 1). Through a comparison with the commercial products, this work offers an advantageous approach for hard tissue repairs.

Figures:

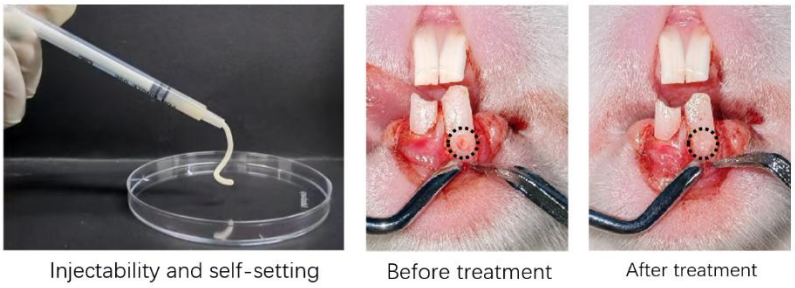

Figure 1. Illustration on the injectability and self-setting characteristic of PolyPIS and its application as dental pulp-capping material.

Key Words: polyphosphate, coacervate, dental pulp, bone repair, self-setting

Mg-dopped Chloride-containing Bioactive Glasses for Bone Regeneration

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Bone defects, frequently stemming from trauma, infections, and congenital anomalies, are prevalent in both dentistry and orthopaedics. Bioactive glasses (BGs) are the most common and widely used synthetic bone substitutes. Chloride containing BGs ($CaCl_2$-BGs) possess excellent biocompatibility and bioactivity and have been proved to facilitate bone formation and integration. However, their potential for clinical applications was limited by the mismatch between the rate of glasses degradation and osseointegration, which is strongly influenced by glass compositions and structure. Mg was reported to facilitate bone formation and the incorporation of Mg in BG could slow down glass degradation. The aims of this work are to develop Mg-dopped chloride silicate BG to achieve a balanced rate between glass degradation and osseointegration and to understand their potential osteogenesis mechanism. All the studied glasses were designed and synthesized by a melt-quench method. The state-of-the-art solid-state NMR, X-ray diffractometer and helium pycnometer were used to characterize the structure of glasses. The effects of adding Mg on glass degradation rate and apatite formation capacity was investigated in Tris buffer solutions. The *in vivo* and *in vitro* osteogenic effects and potential mechanism of the developed BGs were explored. For the *in vivo* experiment a critical-sized full-thickness skull defect model in osteoporotic rats was applied.

The preliminary results showed that the incorporation of Mg slowed down glass degradation meantime accelerated new bone formation. The studied BGs had no cytotoxicity to osteoblasts and macrophages and promoted cell proliferation. *In vivo* experimental results show that Mg-dopped chloride-containing BGs promoted the formation of new bones in osteoporosis rats, and the glass with 10 mol% MgO showed the most pronounced effect. The chloride-containing BGs up-regulated the expression of the RGS1 protein, while down-regulated the expression of downstream key proteins of the G protein-coupled receptor-mediated differentiation of osteoclast IP3-Ca^{2+} signaling pathway. Compared with the Mg free chloride-containing BGs, the influence of the Mg containing ones were more pronounced. In conclusion, Mg-dopped chloride-containing BGs have good bioactivity and biosafety. The incorporation of MgO slowed down glass degradation, while facilitated new bone formation *in vitro* and *in vivo*. The developed BGs are attractive bone substitutes to repair bone defects.

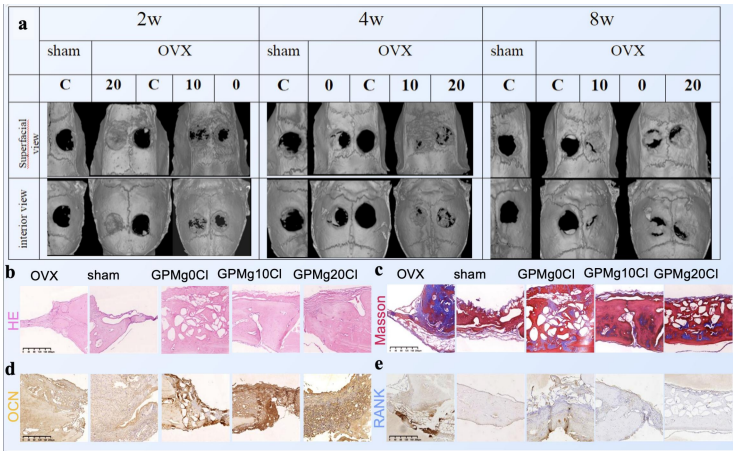

Fig.1 (a)The representative Micro-CT images of the OVX rats skull with defects implanted with/ without BGs for 2, 4 and 8 w. (b) HE staining (c) Masson staining (d) IHC of OCN and (e) RANK of the calvarial defects areas and the interface, the bar is 200 μm. The C, 0, 10 and 20 represent the control, GPMg0Cl, GPMg10Cl and GPMg20Cl group, respectively.

Key Words: Bioactive Glasses, Bone Substitutes, Degradation, Glass structure, Chloride

Boron-modified Alkaline-free Silicate Bioactive Glasses with Anti-inflammatory Properties for bone substitutes

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Macrophage-mediated immune responses are critical to bone regeneration, with moderate polarization toward the M2 phenotype known to enhance osteogenesis [1]. Bioactive glasses (BGs) are promising biodegradable bone graft materials, valued for their unique composition, biocompatibility, and bioactivity. However, conventional silicon-based BGs suffer from limitations such as rapid degradation and limited anti-inflammatory efficacy [2]. In this study, we developed a series of boron-doped bioactive glasses (B-BGs) by incorporating boron into alkali-free silicate BGs. The addition of boron modified the glass network structure, slowed the degradation rate, and promoted the formation of hydroxyapatite (HA). B-BGs demonstrated significant anti-inflammatory effects by downregulating pro-inflammatory markers and upregulating anti-inflammatory cytokines at both gene and protein levels. Furthermore, they facilitated the polarization of macrophages from the pro-inflammatory M1 phenotype to the pro-healing M2 phenotype. In vivo experiments using a rat femoral defect model confirmed that B-BGs improved bone regeneration outcomes by modulating the inflammatory microenvironment and enhancing M2 macrophage polarization. These findings suggest that B-BGs are promising candidates for bone substitute materials with both osteogenic and immunomodulatory capabilities.

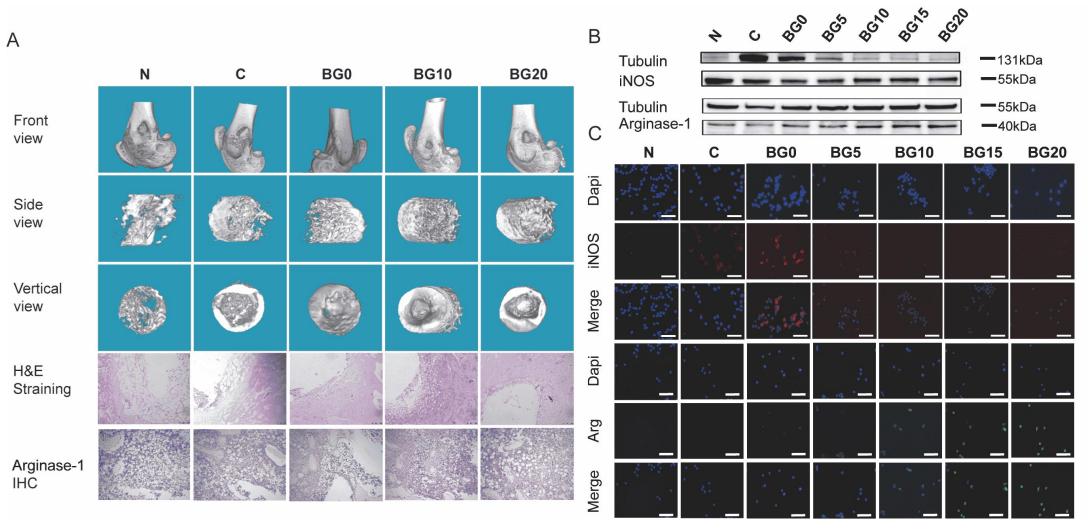

Figure 1. (A) Micro-CT analysis, H&E staining, and immunohistochemical evaluation of bone regeneration in rat femoral condylar defects implanted with B-BGs at 2 and 4 weeks post-surgery. (B) Representative western blot images showing the protein expression levels of iNOS and Arginase-1. (C) Representative fluorescence microscopy images of RAW264.7 cells stained for DAPI (blue), iNOS (red), and Arginase-1 (green).

Key Words: Borate, Bioactive glass, Osteoimmunology, Macrophage, Bone Regeneration

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Incorporating Copper into Fluoride-containing Bioglasses Enhances the Inhibition of Streptococcus Mutans Activity and Biofilm Formation

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Low fluoride-containing bioglasses (LFBGs) with the ability to controllably degrade and form acid-resistant fluorapatite are attractive for caries prevention. However, their antibacterial effect is not satisfactory. To address this problem, we first time incorporated copper (0-5 mol%) into LFBG (1 mol% CaF_2) by a melt-quench method. Then, we investigated the effects of copper addition on the glass structure, bioactivity, cytocompatibility, inhibitory performance against *Streptococcus mutans*, the potential antibacterial mechanism of glasses and cariostatic efficacy *in vivo*. The results revealed that copper was not bound directly to fluoride or orthophosphate and might be present as Si-O-Cu^{2+}. Glasses with the proper copper content (≤ 2 mol%) were cytocompatible. All of the Cu-doped LFBGs (FCuBGs) exhibited high bioactivity, excellent antibacterial properties and superior cariostatic efficacy with increasing copper content. The glasses with the presence of copper significantly inhibited the formation of caries in SD rats. Moreover, we present the first detailed analysis of the potential antibacterial mechanism of FCuBGs, which are attractive for dental applications, including use as fissure sealers, varnishes, and additives for caries prevention.

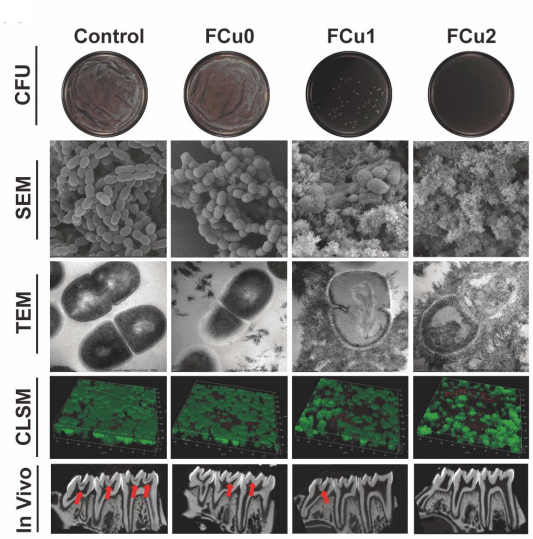

Figure 1. *In vitro* and *in vivo* results of the antibacterial activity of FCuBGs.

Key Words: Copper, Fluoride-containing Bioglasses, Antibacterial, Caries Prevention, *Streptococcus mutans*

Symposia 6

Biomedical Hydrogels

“Restauro” Strategy: Siderophore-Like Antibiofilm Coating Combats Prosthetic Joint Infection and Preserves Implants via Bacterial Ferroptosis-Like Death

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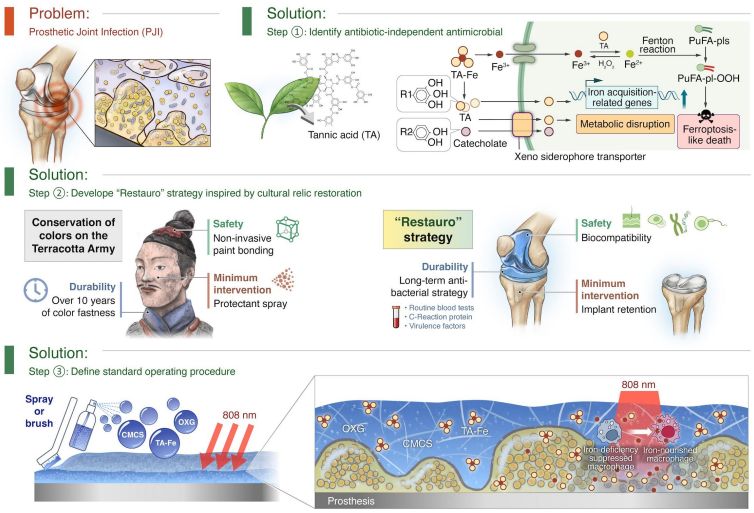
Prosthetic joint infection (PJI) treatment failure primarily stems from incomplete biofilm removal and antibiotic resistance. Addressing these challenges, antibiotic-independent antimicrobials become preferred weapons. Meanwhile, iron metabolism provides an area of interest, due to its essentiality in biofilm formation. Tannic acid (TA), a plant-derived polyphenol, whose siderophore-like antibacterial mechanism is first revealed in this study, leading to ferroptosis-like death in planktonic, biofilm and intracellular bacteria via inducing iron overload. Herein, a novel “Restauro” strategy inspired by cultural relic restoration is proposed to construct CMCS-OXG@TA-Fe (COTF) hydrogels antibiofilm coating. Utilizing the rapid gelation of carboxymethyl chitosan (CMCS) and oxidized xyloglucan (OXG), COTF hydrogels load with TA-Fe complexes, whose photothermal effect can significantly enhance the ferroptosis-like death characteristics and effectively decompose the biofilm structure. Furthermore, COTF can reduce M2 macrophages in iron-deficient microenvironments, remodeling immunosuppression. Eventually, a surgical standard operating procedure (SOP) is developed, which simply requires sequentially brushing or spraying the prosthesis with the fore-mentioned four chemical solutions, in order to achieve antibiofilm efficacy and implant preservation. Eventually, validations in acute and chronic PJI models confirm the preventive and therapeutic effects of “Restauro” strategy, hence building a new bridge from bench to bedside for future PJI treatments.

Keywords: Prosthetic joint infection, Siderophore, Tannic acid, Ferroptosis-like bacterial death, Antibiofilm hydrogel coating.



Biodegradable hydrogel adhesives based on o-phthalaldehyde/amine crosslinking for wound closure and tissue repair

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Medical tissue adhesives are a new class of wound closure materials, which are used as alternatives or adjuvants to sutures owing to the advantages including non-invasive wound closure, ease of application, and excellent sealing performance. In recent studies, we developed a type of biodegradable and biocompatible hydrogels adhesives based on the crosslinking strategy between *o*-phthalaldehyde (OPA) and amino groups (primary amines, hydrazine groups) [1,2]. The tissue adhesion mechanism is based on the fast formation of stable phthalimidine coupling groups between the OPA groups in the hydrogel and the primary amines in the proteins of tissues, leading to rapid wound closure and strong tissue adhesion. In various animal models including full-thickness skin incisions, liver/blood vessel injury bleeding and dura mater defect, the hydrogels can achieve rapid closure of skin incisions, rapid hemostasis of liver and vascular injury, as well as sealing and repair of dura mater defects [2,3].

Key Words: hydrogels, tissue adhesives, wound closure, hemostasis, o-phthalaldehyde/*N*-nucleophile condensation

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Light-responsive pullulan-based hydrogels for spinal tissue regeneration

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Introduction: Spinal injuries and disorders are prevalent in clinical settings, contributing significantly to health complications and socioeconomic burdens. This talk will focus on two specific spine-related pathologies: intervertebral disc degeneration and dural membrane injuries, exploring the use of a pullulan-based hydrogel formulation for the repair and regeneration of these conditions.

Research Design: The talk will cover the development of pullulan-based hydrogels that are functionalized with various bioactive agents, including dopamine, as an adhesive substitute and chondroitin sulfate, as a polyanionic substitute. These hydrogels are designed for spine dural repair and as replacement for the nucleus pulposus in spinal discs. Additionally, the talk will discuss the material chemistry approach used to create photocrosslinkable gels, which enable minimally invasive application at targeted sites.

Results and Discussion: This talk will provide insights into the developed pullulan hydrogel formulation's ability to maintain cell viability and morphological characteristics, indicating its cytocompatibility. The hydrogel's effectiveness in preventing the transition of fibroblasts to myofibroblasts was confirmed using a TGFβ-induced in-vitro anti-fibrotic model. The excellent adhesive performance of the injectable hydrogels in ex-vivo dural tissue underscores their potential for further exploration in spinal applications. The talk will also discuss the tunability of the fixed charge density in the pullulan hydrogels to mimic the polyanionic nature of the nucleus pulposus matrix in the disc. Moreover, the role of high negative charge in the hydrogel in enhancing chondrogenesis by reducing matrix catabolism and improving the expression of anabolic genes such as type II collagen and aggrecan will also be discussed.

Conclusion: In summary, two different injectable formulations of photocrosslinkable pullulan-based hydrogels and their potential utility as an adhesive dural sealant and as a restoration strategy for the nucleus pulposus following disc herniation will be presented. Overall, this engineered hydrogel system offers a promising minimally invasive therapeutic strategy for restoring disc architecture after discectomy and for providing sutureless sealing of dural tears.

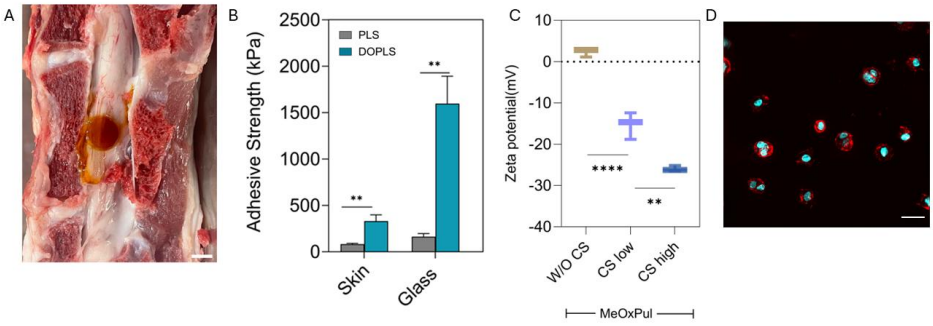

Figure 1: (A) A photograph showing the adhesion of pullulan sealant to the dural surface of the caprine spinal cord. Scale bar: 5 mm. (B) Enhancement of adhesion strength following functionalization with dopamine. (C) Increase in surface negative charge following functionalization with chondroitin sulfate. (D) Morphology of nucleus pulposus cells that are encapsulated within the negatively charged pullulan hydrogel. Scale bar: 50 µm.

Key Words: Injectable hydrogels, Dural Repair, Disc herniation, Pullulan

Acknowledgements: This research is financially supported by the Science and Engineering Research Board (SERB), Government of India (SRG/2022/000712), the Ministry of Human Resource Development, Government of India (STARS-2/2023-0580), and the New Faculty Seed Grant from IIT Madras (IP21221485BTNFSC008985) to GT.

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Engineering multifunctional scaffolds with osteoimmunomodulatory niches for augmented bone regeneration by regulating CCL2/CCR2 pathway

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Developing functional active materials that can mobilize the endogenous regenerative potential of the body and stimulate endogenous bone regeneration has become the direction and frontier of biomaterials science and regenerative medicine. Here, a dynamic hydrogel/bioceramic scaffold with instructive niches is constructed using ceramic 3D-printing technology and biomimetic extracellular matrix strategies. Thereinto, protocatechualdehyde and strontium ions, as organic and inorganic functional elements, are involved in the entanglement of dual-dynamically crosslinked all-polysaccharide hydrogel and mimic cellular active factors. The scaffold orchestrates the multi-scale connecting pore structure for rapid endogenous functional cell infiltration and remodeling the osteogenic immune microenvironment to promote stem cell recruitment, homing and subsequent osteogenic differentiation. Single-cell sequencing analysis as well as its in vitro and in vivo verification demonstrates that the immunoregulatory capacity of bone marrow mesenchymal stem cells (BMSCs) can be enhanced by this scaffold, and promoted the secretion of C-C motif chemokine ligand 2 (CCL2), and effectively bound to the target C-C motif chemokine receptor 2 (CCR2) on the macrophages to activate the M2 phenotype, accelerating endogenous functional cell recruitment and osteogenic differentiation. This work would provide a simple and efficient approach for developing highly active bone regeneration biomaterials.

Key Words: Bone repair; Endogenous bone regeneration; Bioactive scaffolds; Polysaccharide

Acknowledgements: This work was supported by the National Natural Science Foundation of China (22475121), the Huadong Medicine Joint Funds of the Zhejiang Provincial Natural Science Foundation of China (LHDMZ23H300001), the Ningbo Major Research and Development Plan Project (2023Z193), the S&T Innovation 2025 Major Special Program of Ningbo (2019B10063), and the Taishan Scholars Program of Shandong Province (tsqn202306363).

3D Printing and Bioactive hydrogels in Tissue Regeneration Application

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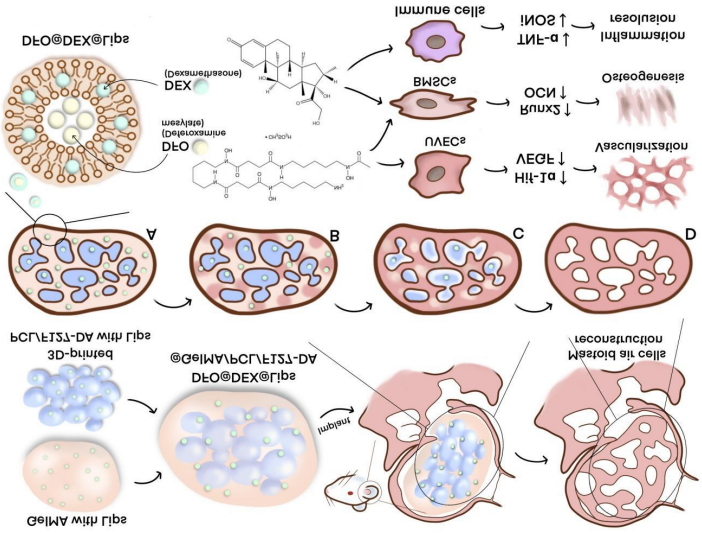
Biological tissue defects are characterized by various defect shapes, susceptibility to bacterial infection, and microenvironmental imbalance, which ultimately makes defect repair and treatment more difficult. 3D printed or dynamically cross-linked bioactive hydrogels can be personalized or adapted to irregular defect areas, supporting and promoting tissue regeneration. The author promoted periodontal tissue regeneration through adjusting drug release time by regulating dynamic chemical bonds in the hydrogel to significantly reduce the inflammatory response. Moreover, the author further introduced mussel-inspired catechol groups into the above self-healing hydrogel to significantly improve tissue adhesion properties, allowing it to fully fill and adhere to irregular tissue defects through injection. In addition, PDA NPs were introduced into the hydrogels to achieve an efficient photothermal antibacterial activity and ultimately promote bacteria-infected wound healing. Finally, ROS-responsive hydrogel was obtained by replacing the above-mentioned dynamic Schiff base chemical bond with ROS-responsive dynamic phenylboronester bond. The introduction of TP@Ag NPs endowed the hydrogel with synergistic and efficient antibacterial properties of photothermal and nano-silver. This hydrogel could fully fill and adhere to irregular wound tissue through injection and significantly promote infected diabetic wound healing in vivo through efficient photothermal synergistic sterilization, ROS scavenging ability and modulation of macrophage M2 polarization to reduce inflammatory response.



Key Words: 3D printing, Dynamic crosslinking, Microenvironmental response, Antibacterial and anti-inflammatory, Tissue repair

Acknowledgements: This research was financially supported by Guangdong Basic and Applied Basic Research Fund Regional Joint Fund-Youth Fund Project, Postdoctoral Science Foundation of China, GDAS' Project of Science and Technology Development, and Guangdong Natural Science Foundation.

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Atomic Insights into Self-Assembly of Zingibroside R1 and its Therapeutic Action Against Fungal Diseases

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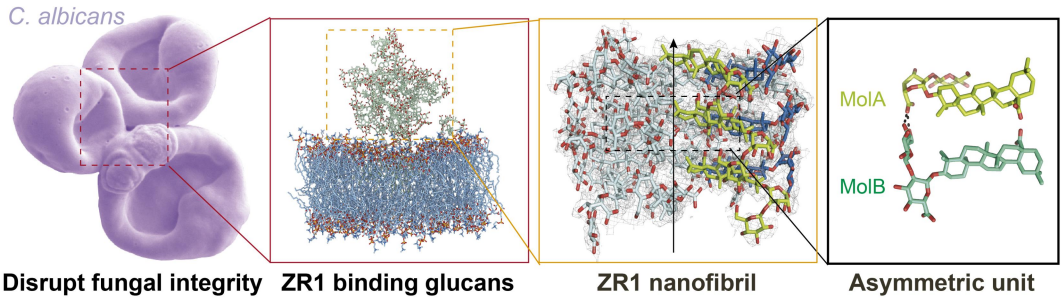
Natural products are a crucial resource for drug discovery, but poor understanding of the molecular-scale mechanisms of their self-assembly into soluble, bioavailable hydrogels limit their applications and therapeutic potential. We demonstrate that Zingibroside R1 (ZR1), derived from Panax notoginseng, undergoes spontaneous self-assemble into a hydrogel comprising helical nanofibrils with potent antifungal activity lacking in its monomeric state. Cryogenic electron microscopy (cryo-EM) revealed an intricate hydrogen-bonding network that facilitates ZR1 nanofibril formation, characterized by a hydrophobic core and hydrophilic exterior architecture, which underpin its binding activity with cell wall in the vulvovaginal candidiasis (VVC) pathogen, *C. albicans*. The hydrogen-bonding interface between ZR1 gel and glucan compromises membrane integrity, inhibiting *C. albicans* proliferation *in vitro* and in VVC model mice *in vivo*. ZR1 gel could also deliver probiotic *Lactobacillus*, synergistically inhibiting VVC and restoring the vaginal microenvironment. This study advances the mechanistic understanding of ZR1's structure-function relationships, offering valuable insights for the rational design and therapeutic optimization of natural product-based hydrogels.



Key Words: natural products, self-assembly, cryo-EM, antifungal, vulvovaginal candidiasis

Acknowledgements: This work was supported by the National Natural Science Foundation of China (32401127); National Youth Talent Support Program (202309460011); Natural Science Foundation of Hunan (2024JJ5072); Science and Technology and Development Foundation of Shenzhen (JCYJ20230807122008016); Hunan Provincial Key Laboratory of Anti-Resistance Microbial Drugs (2023TP1013); State Key Laboratory of Quality Research in Chinese Medicine (005/2023/SKL).

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Mechanical-Electrophysiological Dual-Adaptive Microenvironment Based on Biomimetic Hydrogels Promotes Spinal Cord Injury Repair

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Spinal cord injury (SCI)-induced disruption of central neural conduction networks leads to severe motor dysfunction, significantly impairing patients' quality of life and imposing substantial socioeconomic burdens. Hydrogels hold great potential for neural regeneration due to their biomimetic three-dimensional extracellular matrix structure and tunable mechanical properties.

This study leverages host-guest supramolecular interactions to construct a cell-adaptable ultra-dynamic hydrogel via macromolecular pre-assembly, achieving a stress relaxation rate over 100 times faster than traditional hydrogels to match the mechanical properties of native spinal cord. Furthermore, supramolecular conductive monomers were synthesized using an enzyme-mediated biomimetic strategy, combining supramolecular self-assembly with bio-orthogonal chemistry to fabricate conductive supramolecular hydrogels. Through covalent coupling of β-cyclodextrin and terthiophene, along with glucose oxidase (Gox) and horseradish peroxidase (HRP) cascade catalysis, enzymatic polymerization of polythiophene conductive backbones and hydrogel network formation were synchronized.

The hydrogel demonstrated rapid network reconfiguration, enhancing microparticle mobility (20-fold increased mean square displacement) and enabling 3D neural stem cell migration with 5-fold longer axons. Magnetic field coupling generated in situ electrical pulses within the hydrogel. In beagle SCI models, the hydrogel with wireless stimulation accelerated axonal regrowth and remyelination, restoring standing at 3 weeks and autonomous walking by 12 weeks. This dual-adaptive strategy bridges mechanical and electrophysiological microenvironments, advancing SCI therapeutics. In beagle SCI models, the hydrogel with wireless stimulation accelerated axonal regrowth and remyelination, restoring standing at 3 weeks and autonomous walking by 12 weeks. This study provides a groundbreaking mechanical-electrophysiological dual-adaptive therapeutic strategy for SCI repair, advancing the field of neural regenerative medicine.

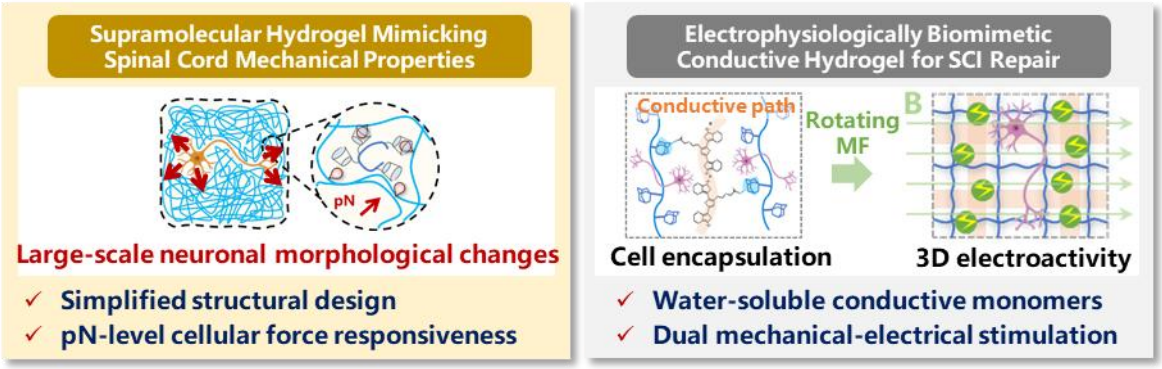

Figure 1. Schematic illustration of biomimetic hydrogels for remodeling the mechanical electrophysiological dual adaptation microenvironment.

Key Words: spinal cord injury; cell adaptable hydrogels; supramolecular interactions; conductivity

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Hydrogel-based Drug and Gas Delivery System for Neuroimmunomodulation in Spinal Cord Injury

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Neuroinflammation following spinal cord injury (SCI) plays a central role in secondary neuronal damage and hinders neurofunctional recovery. The sustained presence of pro-inflammatory microglia/macrophages (M1 phenotype) at the lesion site is a key driver of this process. To address this, we developed a hydrogel-based drug and gas delivery platform that modulates the neuroimmune microenvironment post-SCI. This system integrates minocycline, an anti-inflammatory agent, into a bisphosphonate (BP)-coordinated polymeric hydrogel capable of local, pH-responsive drug release tailored to the acidic SCI milieu. Our results demonstrate that minocycline-loaded hydrogel (MH@BP Gel) effectively inhibit M1 polarization of microglia/macrophages, reduce glial scar formation, and promote neurofilament- and class III β-tubulin-positive neuronal regeneration. Furthermore, incorporating gas-releasing functionality into the BP-based hydrogel further enhanced therapeutic outcomes by not only suppressing M1 activation but also promoting M2-type anti-inflammatory polarization. In vivo studies in a rat SCI model confirmed that this multifunctional hydrogel significantly modulates neuroinflammation, enhances neuronal survival, and facilitates motor function recovery. This work presents a synergistic strategy for targeted neuroimmunomodulation, establishing a promising platform for SCI therapy through localized drug and gas delivery.

Key Words: HA-BP conjugate, Anti-inflammatory macromolecules, Gas-releasing platform, Neuroimmuno-modulation, Spinal cord injury

Acknowledgements: This work was financially supported by the National Natural Science Foundation of China (Grant Number 22275053), the Hunan Provincial Natural Science Foundation of China (Grant Number 2023JJ20005).

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Cell Profiles and Dynamics in the Early Stage of Long Bone Critical-Size Defects Using Hydrogel-Based Scaffolds

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Introduction

Bone defects remain a significant clinical orthopaedic challenge, especially in cases involving large defects that often result in delayed union or non-union. While autogenous bone grafts are the gold standard, their availability is limited. Hydrogel scaffolds provide an ideal environment for cell infiltration and growth, and mesenchymal stem cells (MSCs) have shown promise in enhancing bone defect healing. But the mechanisms by which they interact with the local bone microenvironment are not fully understood. Understanding and modulating these early biological events could lead to novel and robust therapies for improved bone regeneration

Research design

In this study, critical-size femoral defects were created in 10 to 12-week-old BALB/c male mice and stabilized with an external fixation device. Four weeks post-defect, secondary surgeries were performed, and mice were divided into three groups: Empty (no scaffold or cells), Sc (2 mm diameter cylindrical microribbon (μRB) hydrogel scaffold), and Sc+MSC (μRB hydrogel scaffold embedded with MSCs). One week after secondary surgeries, tissues from the defect sites were harvested for single-cell RNA sequencing (scRNA-seq).

Main results

Uniform manifold approximation and projection (UMAP) plots identified cell distributions within the defects, revealing thirteen cell populations annotated using UMAP with Louvain clustering based on marker gene expression. Notable differences in immune cell proportions were observed between the Sc and Sc+MSC groups, with MSCs and osteoblastic lineage cells predominantly found in the Sc+MSC group. Differential gene expression and pathway analysis highlighted immune and inflammatory changes due to MSC implantation, and enhanced cell-cell interactions, particularly among MSCs, macrophages, and T cells, were observed in the Sc+MSC group, with MSCs showing the highest outgoing interaction strength.

Discussion and conclusion

In a critical-size bone defect model, combining MSCs with μRB hydrogel scaffolds increased the presence of mesenchymal lineage cells and promoted the recruitment of macrophages and osteoclasts within one week. This alteration in the local immune landscape could enhance the cellular dynamics crucial for osteogenesis, suggesting that optimizing early cellular crosstalk may improve cell-based therapies using hydrogel scaffolds for bone regeneration in critical-size defects.

Key Words: scRNA-seq, MSCs, bone defect, microribbon hydrogel scaffold

Acknowledgements: This work was supported by the NIH grants R01AR073145 and R01AR063717 from NIAMS, the Ellenburg Chair in Surgery at Stanford University, and the CUHK direct grant for research 399871790 and 488036076.

Enhanced therapeutic potential of a self-healing hyaluronic acid hydrogel for early intervention in osteoarthritis

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Introduction

Osteoarthritis (OA) is characterized by symptoms such as abnormal lubrication function of synovial fluid and heightened friction on the cartilage surface in its early stages, prior to evident cartilage damage. Current early intervention strategies employing lubricated hydrogels to shield cartilage from friction often overlook the significance of hydrogel-cartilage adhesion and enhancement of the cartilage extracellular matrix (ECM).

Research Design

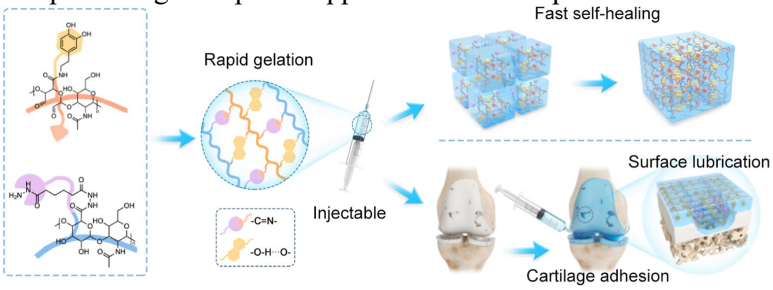
Herein, we constructed a hydrogel based on dihydrazide-modified hyaluronic acid (HA) (AHA) and catechol-conjugated aldehyde-modified HA (CHA), which not only adheres to the cartilage surface as an effective lubricant but also improves the extracellular environment of chondrocytes in OA.

Main Results and Discussion

Material characterization experiments on AHA/CHA hydrogels with varying concentrations validated their exceptional self-healing capabilities, superior injectability and viscoelasticity, sustained adhesion strength to cartilage, and a low friction coefficient. Chondrocytes exhibited robust adhesion and proliferation on the AHA/CHA hydrogel surface, with the upregulation of cartilage matrix protein expression. Intra-articular injection of AHA/CHA hydrogels was performed following destabilization of the medial meniscus (DMM) surgery in mice to assess its protective effect on cartilage.

Conclusion

The AHA/CHA hydrogel effectively attenuated the degree of cartilage wear, facilitated chondrocytes' anabolic metabolism, and restored the ECM of cartilage. Therefore, the AHA/CHA hydrogel emerges as a promising therapeutic approach in clinical practices of OA treatment.



Key Words: Osteoarthritis, hyaluronic acid hydrogel, self-healing, injectability, cartilage surface friction

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Basic Research and Clinical Application of Ordered Collagen Scaffolds Combined with Human Neural Stem Cells to Promote Spinal Cord Injury Repair and Regeneration

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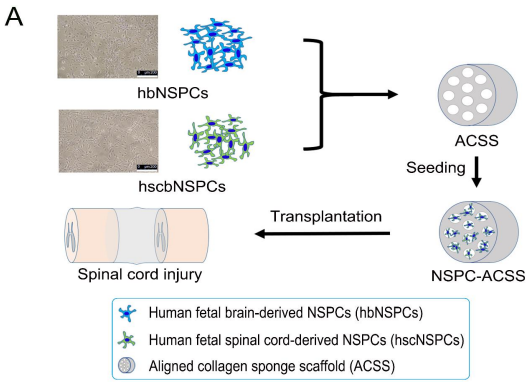
Introduction Biomaterial scaffolds combined with neural stem cells (NSCs) offer a promising strategy to repair of damaged spinal cord tissue and promote functional recovery. While ordered collagen scaffolds provide structural guidance for axonal regrowth.

Research Design Ordered collagen scaffolds loaded with fetal spinal cord-derived NSCs were implanted into the lesion site. Histological, functional, and microenvironmental outcomes were assessed over 8 weeks. A pilot clinical trial was conducted on one patient with acute complete SCI.

Main Results and Discussion The scaffold-NSC composite effectively promoted long-term cell survival and neuronal differentiation and improved the SCI microenvironment by reducing inflammation and glial scar formation. Clinical research: After 24 months, the patient achieved bilateral iliopsoas muscle strength recovery to grade 3 and partial sensory improvement, demonstrating functional restoration.

Discussion The ordered collagen scaffold mimics native spinal cord alignment, synergizing with NSCs to modulate the inhibitory microenvironment. Clinical outcomes highlight translational potential.

Conclusion This study establishes ordered collagen scaffolds combined with fetal spinal cord-derived NSCs as a safe and effective strategy for acute complete SCI repair. This novel and effective method shows promise for application in biomaterial scaffold and cell-based therapy for SCI in the future.



Key Words: Ordered Collagen Scaffolds, Neural Stem Cells, Spinal Cord Injury, Regeneration

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Symposia 7

Biomaterial Pre-clinical and Clinical Trials

POLYSACCHARIDE-BASED NANOFORMULATIONS FOR CARDIAC RNA-BASED THERAPEIS: FROM NANO-DESIGN TO *IN VIVO* APPLICATIONS

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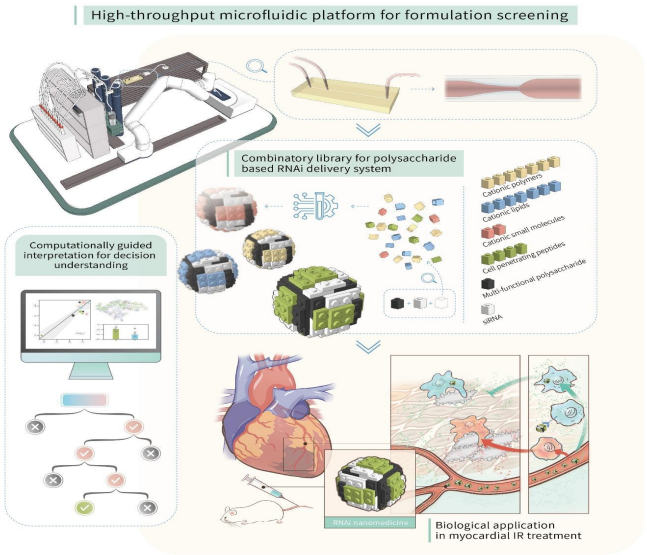
Cardiovascular diseases (CVDs) remain the leading cause of mortality globally. Nanotechnology has emerged as a transformative strategy for targeted drug delivery via rational design. Yet, challenges persist, such as ischemic myocardium and lesional plaques. To address these, polysaccharide- and metal-organic frameworks-based nanosystems can be used achieve precise drug delivery towards the conditioning of myocardial ischemic injury/atherosclerosis [1-3]. Here, I will present our latest works on the abovementioned nanosystems demonstrated selective affinity towards lesional macrophages, driven by interactions with the Dectin-1 receptor. Functional heart evaluation using clinical-relevant murine models were conducted, demonstrating that these type of nanosystems can mitigate ischemia-reperfusion injury and inflammatory responses. Overall, we have demonstrated that different nanomedicines directed to specific cells and cell-receptors need to be carefully designed and optimized, promoting the development of precision medicine for CVDs, highlighting their clinical translational potential.



Key Words: Nanomedicine, beta-glucans, myocardium infarction, cardiovascular diseases, targeting

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Medicine-Engineering Interdisciplinary Research based on Innovation and Industrialization of High-end Biomedical Materials

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As a global strategic development industry, biomaterials are widely used in medical devices, pharmaceutical preparations, aesthetic medicine, diagnostic reagents and other fields. Our group has carried out the medicine-engineering interdisciplinary research and industrialization of guide tissue regeneration (GTR) biomaterials since 1990, and have obtained 9 registrations of class III medical devices, medical device export license, ISO certification, CE certification, FDA certification, Russian certification, UK certification, etc. Medical collagen membrane and medical collagen repair membrane have been applied in more than 500 hospitals across the country in stomatology, orthopedics, ophthalmology, plastic surgery, Neurosurgery and other applications without any adverse medical events. Spongious bone substitute is the first approved bone substitute made by discarded marine shell, and the related technologies have led the international frontier and created a new international track for Marine biomedicine and created a new international track of marine biomedicine. New Coronavirus (2019-nCoV) Antibody Detection Kit has exported to the United Kingdom, Russia, Vietnam and other countries to help the international epidemic prevention and control. Recently, GTR biomaterials have been widely used in the fields of tissue construction and organ regeneration. The essence of scientific research is to pursue the ultimate application, and theoretical innovation or basic research is valuable to clarify the mechanism and lay the foundation for technological innovation and practical application. There are still unresolved scientific problems in the world today. Scientists from all countries need to work together to solve medical problems and integrate Industry-University-Research to promote the development of human health.

Keywords: medicine-engineering interdisciplinary, Industry-University-Research, medical devices, Marine biomedicine

Symposia 8

Biomaterials for Nanomedicine and Tissue Engineering

Role of Chiral MoS_2 Nanocomposite Membrane in Bone Regeneration

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Introduction: One of the critical challenges in current barrier membrane materials for dental implant surgery lies in maintaining defect alveolar bone space stability as a physical barrier while simultaneously delivering osteoinductive activity and antibacterial potential within a specific timeframe [1]. Molybdenum disulfide (MoS_2) nanomaterials exhibit excellent antibacterial properties; chirally engineered materials enhance cellular uptake and enable controlled drug or gene delivery; quantum dots (QDs) can integrate with drug molecules to form multifunctional nanocarriers for efficient drug loading and targeted delivery via surface functionalization [2].

Research design: To address these challenges, we synthesized chiral MoS_2 QDs via a hydrothermal method and fabricated a chiral MoS_2 QDs-based bilayer nanocomposite membrane using self-evaporation and spray-coating techniques.

Results: Scanning electron microscopy confirmed that the rough surface of the membrane promotes osteoblast recruitment, while the smooth surface inhibits fibroblast and bacterial adhesion. In vitro osteogenic induction and in vivo calvarial defect models demonstrated that the L-MoS_2 QDs-based bilayer membrane exhibits robust osteoinductive capacity. Both in vitro and in vivo experiments further validated its superior antibacterial performance.

Conclusion: The developed L-MoS_2 QDs bilayer nanocomposite membrane, with its dual functionality of osteogenesis promotion and bacterial inhibition, offers a promising theoretical and experimental foundation for advancing clinical bone regeneration materials in implant dentistry.

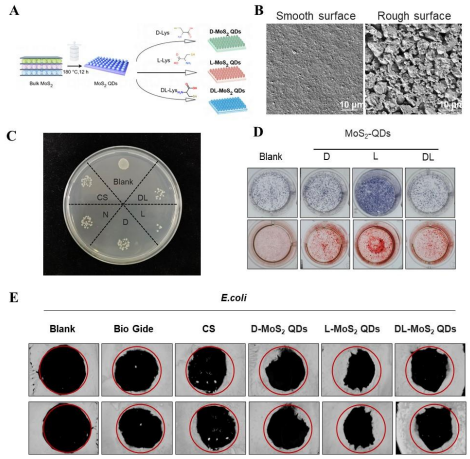

Figure legend: A. Schematic illustration of the synthesis strategy for MoS2 QDs; B. Scanning electron microscopy (SEM) images of the MoS2 QDs-based bilayer nanocomposite membrane, showing the smooth surface (left) and rough surface (right); C. Antibacterial performance of various groups of nanocomposite membranes; D. In vitro osteogenic induction performance of different groups of nanocomposite membranes; E. In vivo evaluation of antibacterial and osteogenic capabilities of the nanocomposite membranes in a rat calvarial defect model with concomitant E. coli infection.

Key Words: Molybdenum disulfide, Quantum dots, nanocomposite membrane, antibacterial, osteogenesis)

Acknowledgements: This work was supported in part by grants from the National Natural Science Foundation of China (NSFC) [82401064, 82101048]

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Drug-Free Extracellular Vesicles: A Novel Spatiotemporal Controlled Release Engineering Strategy for Osteogenesis and Anti-Inflammatory Microenvironment in Rotator Cuff Regeneration

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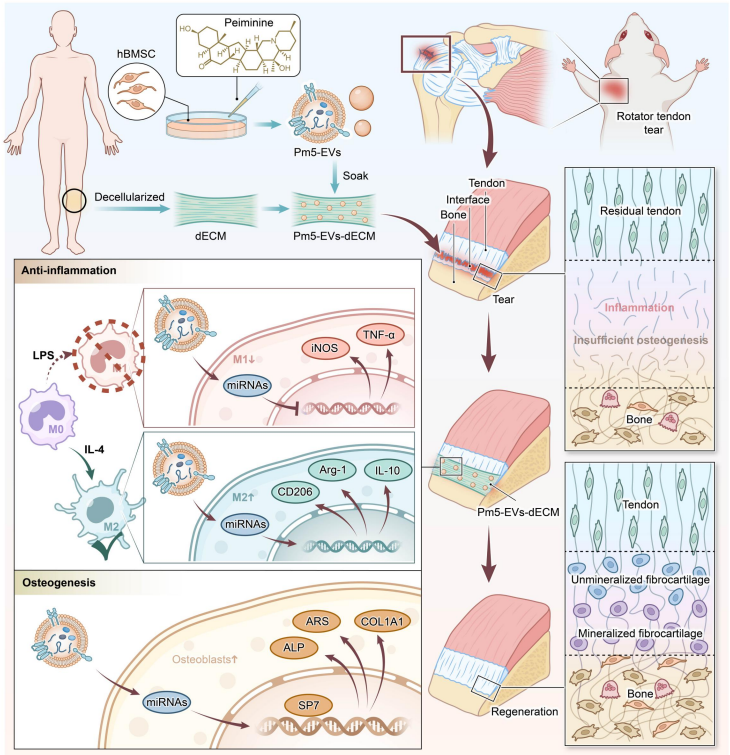
Natural small molecule drugs have potential in tissue regeneration, but there's a need to balance efficacy and side - effects. Peiminine, from Fritillaria, has osteogenic and anti - inflammatory effects in bone regeneration but is limited by low bioactivity and poor biocompatibility. This study developed a drug - free bioengineering method for rotator cuff regeneration. It used BMSCs, dECM, and a rat rotator cuff injury model. BMSCs were pretreated with Peiminine, and the secreted Peim - EVs were combined with dECM to form an EVs - dECM system. In vitro, Peim - EVs' properties and related pathways were studied; in vivo, the system's effect on rotator cuff repair was evaluated. Results showed Peim - EVs overcame Peiminine's biocompatibility problem and had osteogenic and anti - inflammatory effects, possibly related to certain pathways. The EVs - dECM system promoted rotator cuff repair, improved tendon - bone interface properties, and had better mechanical properties than the direct repair group. In summary, the EVs - dECM system makes Peim - EVs inherit Peiminine's beneficial properties. This study provides a new tissue regeneration strategy with clinical significance.



Key Words: Drug-free extracellular vesicles; Rotator cuff regeneration; Spatiotemporal controlled release; Peiminine; Osteogenesis and anti-inflammation.

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Development of elemental technologies for a new platform for creating practical Whole Organ Engineered-Livers

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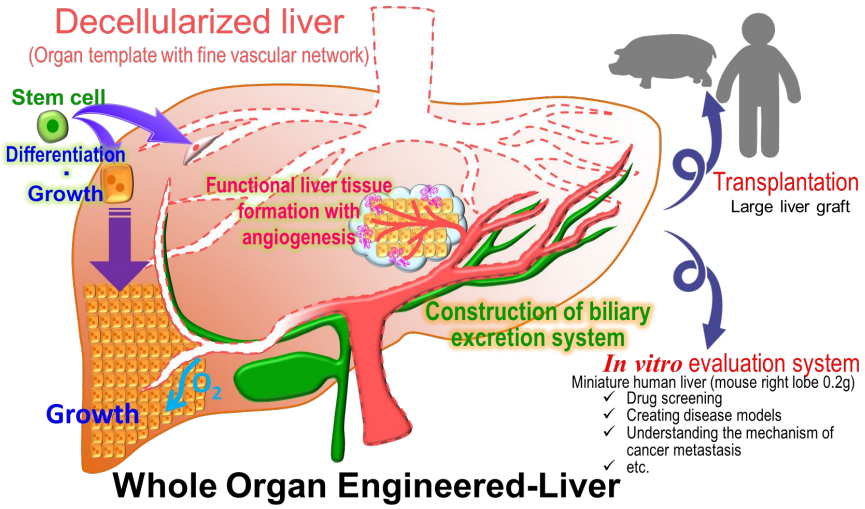
The liver is the central organ of metabolism in the body, and resolving the chronic donor shortage is a serious global issue. Whole Organ Engineered-Liver, which is composed of cells, functional ECM, and scaffolds with fine vascular-tree networks, has high potential for the creation of highly functional liver grafts for transplantation [1], but various efforts are required to further improve its performance. Here, the challenges to be solved and their solutions will be presented.

(1) Cells: Treatment with a combination of trehalose and its derivatives enabled the cryopreservation of healthy primary hepatocytes [2]. In addition, PEGylated GRGDS suppressed apoptosis of primary hepatocytes during seeding, achieving good cell survival rates and high liver function expression [3]. (2) Organ culture system: An organ culture system with an appropriate oxygenation system and an organ shape retention device was developed, making it possible to maintain and culture healthy livers. This realized the development of hardware for liver graft creation. (3) Support technology: Biocompatible nanogel particles reduced ischemia-reperfusion injury in liver grafts. In other words, the development of technology to support the success of regenerative medicine was successful.

The integration of conventional Liver Tissue Engineering with the various problem-solving technologies mentioned above is expected to become a new platform for creating practical Whole Organ Engineered-Livers.



Key Words: Whole Organ Engineered-Liver, PEGylated GRGDS, Nanogel particle

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Supramolecular Self-Assembled Polymers and Hydrogels for Nanomedicine and Sustainability Applications

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Supramolecular host-guest chemistry utilizing cyclodextrins has offered a convenient and powerful approach for constructing complex nanostructures from tunable molecular building blocks. Over the past two decades, our research group has focused on creating novel self-assembled polymeric micro- and nanostructures using both biobased and synthetic polymers. These polymer blocks have been engineered to form responsive structures, including hydrogels, micelles, nanovesicles, and surface coatings, which are applied in biomedicine[1,2] and sustainability[3].

One of the main challenges in drug and gene delivery is designing multifunctional carrier systems that enhance delivery efficiency, often requiring complex multistep synthesis. Our approach leverages the host-guest chemistry of cyclodextrins to create adaptable carrier systems. We developed a structure combining a β-cyclodextrin-based cationic host polymer with a range of guest polymers of varying PEG shapes and ligand densities. The host polymer encapsulates siRNA, ensuring controlled loading and release, while the guest polymers enhance biocompatibility by preventing nonspecific cellular uptake and improving circulation time. This streamlined assembly process generates siRNA delivery vehicles with precisely controlled architectures, enabling rapid optimization for targeted delivery in vitro and in vivo. Our findings demonstrate a strong correlation between in vitro and in vivo results, highlighting the effectiveness of this supramolecular method as a screening tool for targeted gene delivery vehicles.

In another work, we developed a sharp-contrast Janus star polymer (SJSP) consisting of multiple arms of superhydrophobic lipid moieties and superhydrophilic polyzwitterion chains attached to a β-cyclodextrin core. The SJSP polymer forms nanomicelles possessing a stable core and a controllable and dense stealth shell that effectively protects them in the bloodstream, preventing payload leakage and blood protein adsorption. The SJSP micelle system shows significantly longer blood circulation time in vivo compared to linear counterparts and other available amphiphilic block copolymer micelle systems.

Key Words: Drug Delivery, Gene Delivery, Hydrogel, Micelle, Superabsorbent Polymer

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LEGO®-inspired Modular Bioinks for 3D Bioprinting *In Vitro* Models

Ke Zhou[1], Yiwei Jia[1], Yuting Zou[1], Yuting Wen[1,2], and Jun Li[1,2]

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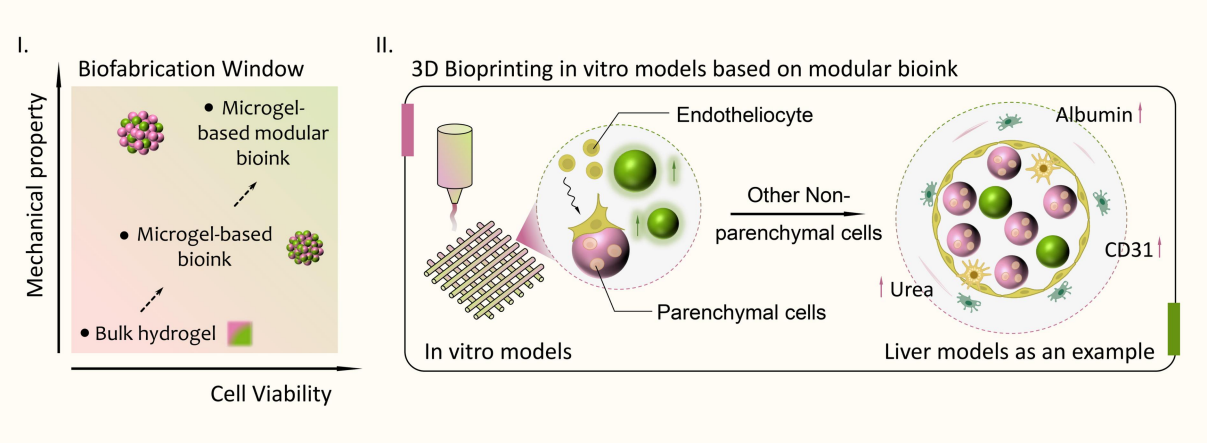
3D bioprinting has emerged as a cutting-edge approach for constructing *in vitro* models. Despite its tremendous potential, suitable bioinks that meet the conflicting requirements for biocompatibility and printability still remain unidentified. In our previous work, we engineered a dendrimer-reinforced bioink [1] and photoclick polysaccharide-based bioink [2] to extend the Biofabrication Window. Here, we present a novel strategy that utilizes natural polymer-derived microgels (gelatin methacryloyl, GelMA) and size-matched synthetic microgels (polyethylene glycol diacrylate, PEGDA) to assemble LEGO®-inspired modular units, which combine with another phase of hydrogel precursor solution to form a biphasic modular bioink. Through meticulous adjustment of the volume ratio between natural and synthetic microgels within the modular system, the mechanical properties of 3D bioprinted in vitro models can closely approximate those of *in vivo* soft tissues. In contrast to conventional bulk hydrogel and composite microgel-based bioink, cells encapsulated within this system exhibit selective adhesion to natural microgel surfaces, accompanied by pronounced spreading behavior that enhances cell viability. Moreover, this bioink supports heterogeneous cell encapsulation, allowing co-localization of parenchymal and non-parenchymal cells to recreate tissue-specific microenvironments. We demonstrate that such spatially patterned architectures promote cellular self-organization and vascularization, ultimately augmenting hepatic functionality. Altogether, this new LEGO®-inspired paradigm can be developed that harnesses the unique edges of natural and synthetic microgels to resolve the trade-offs of traditional bioinks, which widely broadens the Biofabrication Window and boosts the application prospects of 3D bioprinting for in vitro models.



Key Words: 3D bioprinting, Bioink, Microgel, Liver models, Biofabrication window

Acknowledgements: This work was supported by the Science and Technology Project of Jiangsu Province (BZ2022056).

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A Wound Exudate-Activated Yarn Battery for Antimicrobial Electrical Fabric Dressing

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Excessive inflammation poses a major challenge to wound care, with massive exudation and bacterial infection being the prominent factors contributing to the inflammation[1]. Currently, research on excessive exudate from wounds mainly focuses on physical removal[2],with less attention given to the benefits of exudate for the wound and its effective utilization. The basic components in the exudate can provide nutrients for cell migration and growth[3], while the water and ions in the exudate also hold promise for therapeutic purposes. Inspired by the endogenous electric field (EF), the present study developed an antimicrobial and self-powered electrical fabric dressing (EFD). An EFD with multifunctional properties of wound exudate collection, anti-infection, and self-powered electrical stimulation (ES) was assembled via weaving a series of hydrophilically modified cotton yarn-based batteries. Upon contact with the wound, EFD absorbs the wound exudate owing to its high hydrophilicity and utilized the exudate as the natural electrolyte to activate the battery. With the endogenous power supply, the ES-promoted polarization of macrophages, as well as the migration and proliferation of fibroblasts, enhancing the active wound repair process. Moreover, the dressings exhibited excellent antibacterial properties, attributable to the synergistic effects of the cationic polymer brushes on the cotton yarn and the anodic by-product (magnesium hydroxide) during discharging. Thus, the wound exudate-activated EFD could effectively manage wound exudates, prevent bacterial infection, and provide self-powered electrotherapy to facilitate active wound tissue repair.

Key Words: Wound exudate-activated yarn battery, electronic fabric dressing, endogenous electric field, active wound repair, antibacterial

Acknowledgements: This research was supported by the National Key R&D Programmes of China (2022YFE0140300), National Natural Science Foundation of China (U24A20511, 52073234 and 22378335), Fundamental Research Funds for the Central Universities (SWU-XJPY202304), and Chongqing Engineering Research Center for Micro-Nano Biomedical Materials and Devices. We are grateful for the assistance of Dr.

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Dual-Targeting Liposome against Acne through Coordinated Microbial Eradication and Inflammatory Pathway Inhibition

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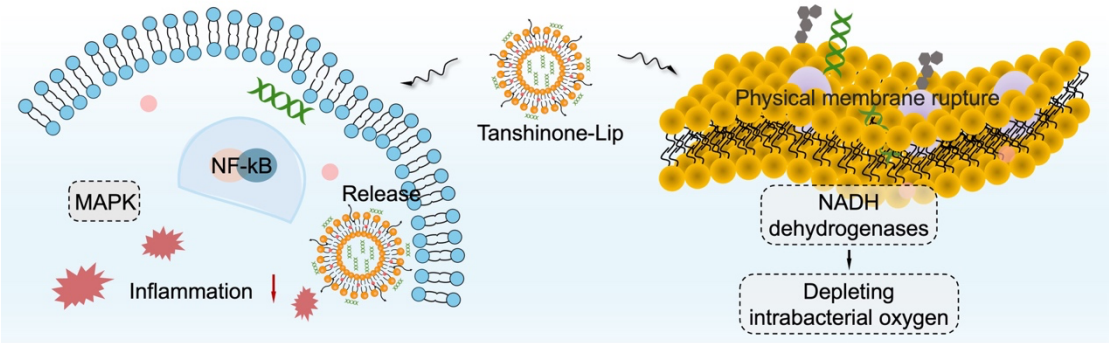
Acne vulgaris, the second most prevalent dermatological disorder globally, remains inadequately managed due to safety concerns and limited efficacy of current therapies. To overcome these challenges, a dual-modified liposomal nanocarrier [1, 2] co-loaded with tanshinone (Tanshinone-Lip), is engineered for acne treatment via simultaneous bacterial eradication and inflammatory response inhibition. Tanshinone-Lip possesses excellent antimicrobial activity through two mechanisms, physical disruption of bacteria membrane and targeted inhibition of NADH dehydrogenases. In inflammatory cells, Tanshinone-Lip markedly inhibited the phosphorylation of mitogen-activated protein kinase (MAPK) and nuclear factor-kappa B (NF-κB) activation. Notably, in infection models, Tanshinone-Lip exhibited superior efficacy against intracellular multidrug-resistant pathogens, achieving over 60% bacterial clearance compared to control group (p<0.01). These findings establish a novel combinatorial strategy through rational nanocarrier design, providing a promising translational solution for acne pathophysiology modulation via coordinated antimicrobial and anti-inflammatory actions.



Scheme. Schematic illustration of the dual-targeting liposome system for acne treatment.

Key Words: dual targeting nanoplatform, liposome, tanshinone, acne

Acknowledgements: This work was supported by the Science and Technology Project of Jiangsu Province (BZ2022056).

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Combined 3D microfluidic vortex focusing and high-throughput screening for self-assembly synthesis of homogeneous nanomedicine

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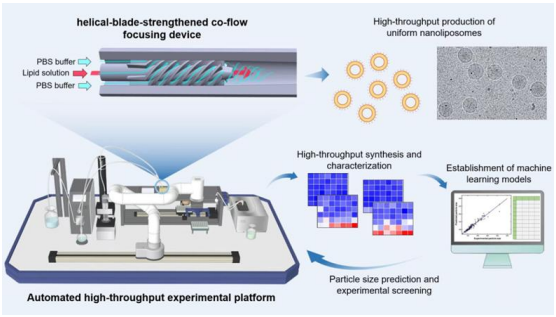
Nanoliposomes have been widely employed as promising drug delivery vehicles for the treatment of various diseases. However, the large-scale synthesis of drug-loaded nanoliposomes manifesting a highly uniform particle size is impeded by several unmet challenges. Herein a novel helical-blade-strengthened co-flow focusing (HBSCF) device was developed by installing multiple parallel helical blades in a commonly used co-flow focusing microfluidic device. This transformation in the microchannel structure may accelerate the mixing of aqueous and lipid streams in a radial direction, thereby affording the production of nanoliposomes with a significantly lower polydispersity index (PDI) value in terms of particle size. Moreover, a high-throughput experimental platform was developed by employing HBSCF device alongside its integration with various automation modules. Afterwards, based on the obtained large data set of nanoliposomes, a typical machine learning (ML) model pertaining to particle size was established to predict candidate synthesis schemes for the desired average particle size. Therefore, by narrowing the screening ranges through ML, the final synthesis scheme capable of producing liposomes with the desired particle size along with minimum PDI value can be precisely and rapidly obtained using automated experiments based on the same platform. Taken together, an effective integration of the HBSCF synthesis along with an automated high-throughput experimental platform may have broad implications for the industrialization and clinical application of nanomedicine.[1,2]



Key Words: microfluidics; high-throughput synthesis; nanomedicine

Acknowledgements: This work was supported by National Natural Science Foundation of China (Grant No. 52072392), Youth Innovation Promotion Association CAS (Grant No. 2020255), the Shanghai Science International Cooperation Project (Grant No. 23490712900).

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On the Development of Hypoxia-mimicking and Immuno-regulatory Polycaprolactone (PCL)-based Small-diameter Vascular Grafts for *In Situ* Blood Vessel Regeneration

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Introduction: Cardiovascular diseases cause huge morbidity and mortality worldwide. Whereas, artificial vascular grafts demonstrate satisfactory performance in large-caliber arteries, they show poor patency when used as small-caliber substitutes.[1-3] The objective of this research was to evaluate the potential of loading bioactive molecules, dimethyloxalylglycine (DMOG) or Fingolimod (FTY720), on *in situ* vascular regeneration in polycaprolactone (PCL)-based vascular grafts.

Research design: PCL-based small-diameter vascular grafts containing DMOG or FTY720 were fabricated by electrospinning. The grafts were evaluated for morphology, mechanical characteristics, hemocompatibility, and cell compatibility (**Fig. 1**). Moreover, vascular grafts with or without DMOG and FTY720 loading were transplanted as abdominal aorta substitutes in rats and as carotid artery substitutes in mice and rabbit models, for up to 4 weeks, respectively. Explants were characterized by SEM observation for endothelialization and alongside histological and immuno-histochemical assays.

Results and Discussion: Morphological, biomechanical, and blood compatibility of PCL grafts were not influenced by the addition of DMOG or FTY720. The migration of human umbilical vein endothelial cells (HUVECs) was increased in DMOG- or FTY720-loaded vascular grafts. Moreover, the lumen of DMOG- or FTY720-loaded grafts was covered by ECs, whereas instances of free voids were observed on the luminal side of bare PCL grafts. DMOG- or FTY720-loaded vascular grafts also exhibited more number of capillaries in the graft wall as well as showed the infiltration of a substantial number of anti-inflammatory (M2) macrophages than that of the PCL-only group.

Conclusion: Taken together, hypoxia-mimicking and immuno-regulatory vascular grafts may be harnessed for the development of off-the-shelf vascular grafts for cardiovascular tissue repair.

Key words: (artificial vascular grafts, vascular regeneration, immunomodulation, electrospinning)

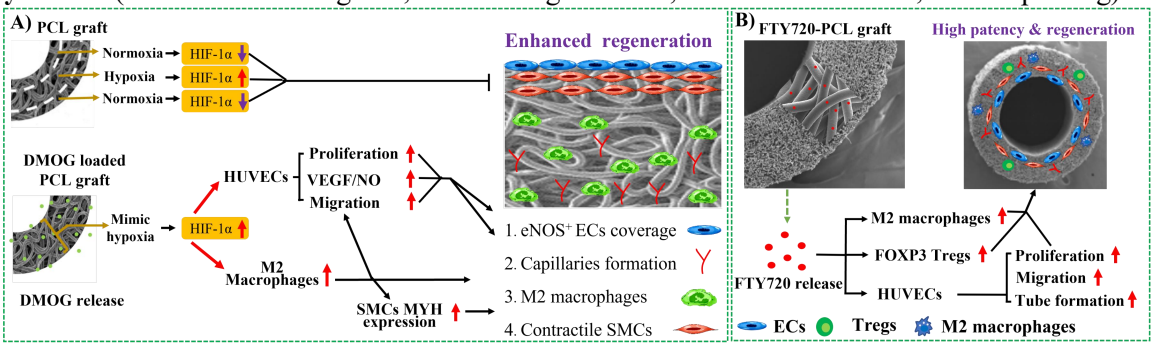

Figure 1. Schematic illustration of regenerative and immunomodulatory effects of DMOG and FTY720 loading for *in situ* blood vessel regeneration in PCL-based vascular grafts.

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Imparting Multifunctionality to Polymeric Biomaterials and Harnessing Nature's Wisdom to Promote Biocompatibility of Medical Implants for Regenerative Medicine and Tissue Engineering

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Introduction: Biocompatible and biodegradable polymers are at the forefront of the biomedical research albeit the lack of cell recognition motifs and extracellular matrix (ECM)-mimetic morphological cues. Bulk modification of polymers with functional handles as well as the incorporation of decellularized extracellular matrix (d-ECM) and hierarchical cues into biomaterials may offer an enticing platform to improve implants' biocompatibility and induce neo-tissue formation.

Research design: Linear and star-shaped poly(L-lactide-co-*ε*-caprolactone) (PLCL) copolymers were synthesized by ring-opening polymerization (ROP), modified with stem cell inducing/recruiting peptides, and electrospun to fabricate fibers and small-diameter vascular grafts.[1-2] Functional peptides-loaded vascular grafts and cardiac patches were prepared using co-electospinning, while skin equivalents with co-axial electrospinning. Similarly, core/shell type aligned electrospun fibers were prepared using PCL and gelatin (Gel) or Gel along with brain-derived ECM (B-ECM) to fabricate nerve guidance conduits (NGCs). Biofunctionalized polymers were comprehensively analyzed, while vascular grafts, cardiac patches, skin equivalents, and NGCs were studied *in vitro* and *in vivo*.[3-4]

Results and Discussion: Linear and star-shaped PLCL copolymers were successfully synthesized and modified in bulk. Bioactivated polymers recruited stem cells *in vitro* and *in vivo* as well as promoted selective capture of mesenchymal stem cells (MSC) and endothelial progenitor cells (EPCs). Vascular grafts containing bioactive polymers showed higher infiltration of host cells, regeneration of confluent endothelium, vascular remodeling, and higher patency rate as abdominal aorta substitutes in rats. Peptides-loaded grafts and cardiac patches recruited host stem/progenitor cells *in vitro* and *in vivo*. Vascular grafts containing stromal cell-derived factor-1-alpha (SDF-1α) and prominin-1-derived peptide (PR1P) also recruited Sca-1^+ cells *in vivo*. Heparin-conjugated growth factor (GF)-immobilized fibers promoted GFs retention *in vivo*, while B-ECM-based aligned fibers enhanced the migration and neurite outgrowth of Schwann cells and Pheochromocytoma (PC12) cells in a dose-dependent manner both in the soluble form as well as immobilized form in fibers. NGCs containing immobilized GFs and B-ECM showed higher biocompatibility in a sciatic nerve defect model.

Conclusions: Bioactive elastomeric polymers can promote *in situ* tissue regeneration via enhanced mobilization and recruitment of host stem/progenitor cells. Functional peptides, such as neuropeptide substance P (SP), SDF-1α, IGF-1C-derived peptide, and PR1P can be successfully loaded into co-electrospun and co-axial fibers and released in a sustained manner. GFs-immobilized and B-ECM-based core/shell fibers can promote neuronal cell capture, axonal extension, and nerve tissue repair.

Key words: (artificial vascular grafts, vascular regeneration, nerve regeneration, electrospinning)

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Dual-grafted dual-network hydrogel system promotes synergetic regeneration of heterogeneous interfaces

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Rotator cuff injury repair faces challenges such as insufficient blood supply at the tendon-bone interface, an inflammatory microenvironment, and limited bone regeneration capacity.

In this study, a novel bifunctionalized mesoporous bioactive glass (A-MBG) grafted with α-ketoglutarate (α-KG) and adenosine was designed. It was integrated into a methacryloylgelatin/methacryloylhyaluronic acid (GelMA/HAMA) bi-networked hydrogel scaffold (A-MBG@GH). The mesoporous structure and surface functionalization of A-MBG were systematically characterized, and its slow-release properties and biocompatibility were investigated.

In vitro, A-MBG promoted the osteogenic differentiation of bone marrow mesenchymal stem cells, inhibited the M1-type pro-inflammatory polarization of macrophages, and enhanced the angiogenesis of endothelial cells. The GelMA/HAMA hydrogel scaffolds ensured the slow release of drugs and the in-situ migration of cells through their porous structure and mechanical support properties. In vivo, in a rat rotator cuff injury model, A-MBG@GH promoted the physiological healing of the microstructure at the tendon-bone interface. It significantly improved histological scores, collagen tissue maturation, and biomechanical properties through bone regeneration, modulation of the inflammatory microenvironment, and angiogenesis. Molecular docking and immunohistochemical techniques predicted the mechanism by which adenosine binds to α-KG to achieve its biological function, that is, by binding to MAPK1 to promote its activation.

The combination of α-KG and adenosine in A-MBG enhanced its bioactivity. The GelMA/HAMA hydrogel scaffold provided a suitable environment for drug release and cell behavior. The findings of this study are of great significance for understanding the treatment of rotator cuff injuries.

This study provides an innovative solution for complex tissue interface regeneration by integrating osteogenesis, angiogenesis, and anti-inflammation into a single A-MBG composite GelMA/HAMA scaffold strategy. It has both mechanistic depth and clinical translational potential, opening up a new direction for the field of rotator cuff injury repair.

Key Words: Rotator cuff tear, Tendon-to-bone interface, Adenosine, α-Ketoglutaric acid, Hydrogel

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Cyclodextrin-Based Supramolecular Delivery Systems for Near-Infrared Dye-Mediated Diagnosis and Photothermal Therapy

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Cyclodextrin (CD)-based supramolecular platforms offer a promising approach for the delivery of diagnostic and therapeutic agents due to their well-defined host-guest chemistry, biocompatibility, and modular design. We developed a series of CD-based delivery systems, including CD-crosslinked nanogels and poly(cyclodextrin)-grafted polymers, to encapsulate near-infrared (NIR) dyes such as indocyanine green (ICG) and other NIR fluorophores for applications in fluorescence imaging and photothermal therapy (PTT). These systems utilize non-covalent CD-guest interactions to achieve stable dye loading and enhanced photophysical properties.

Our results demonstrate that these supramolecular carriers improve dye solubility, photostability, and bioavailability, enabling an enhanced signal-to-noise ratio in imaging and efficient PTT in vitro and in vivo. Furthermore, CD-based platforms are engineered to co-deliver chemotherapeutic agents or immunomodulators, establishing a synergistic strategy that combines PTT with chemotherapy or immunotherapy. Combinational studies reveal improved therapeutic efficacy and immune activation in mice tumor models.

These findings exhibit the potential of CD-based nanoplatforms as multifunctional platforms for integrated diagnostic and therapeutic applications (theranostics), providing a flexible and translatable strategy for NIR-guided cancer diagnosis and treatment.

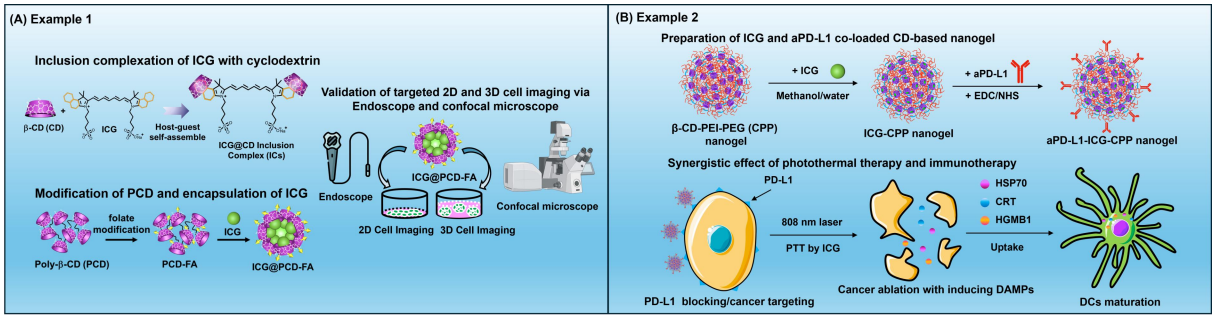

Figure 1. Cyclodextrin-based supramolecular systems for near-infrared dye delivery and multifunctional biomedical applications. (A) Example 1: Schematic illustration of the inclusion complexation of indocyanine green (ICG) with poly-β-cyclodextrin (PCD), modified with targeting ligand folate (FA). These supramolecular constructs enable efficient ICG encapsulation and facilitate 2D and 3D cell imaging via endoscopy and confocal microscopy. (B) Example 2: Preparation of a CD-based nanogel co-loaded with ICG and anti-PD-L1 (αPD-L1). The nanogel enables combined photothermal therapy (PTT) and immunotherapy through synergistic effects, including PD-L1 blockade, cancer ablation, and immune system activation.

Key Words: cyclodextrin, supramolecular assembly, NIR fluorescence, diagnosis, photothermal therapy

Acknowledgements: National Natural Science Foundation of China (grant no. 82202315)

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Vascular Endothelial Growth Factor and Endogenous Calcium-Capturing Hydrogels Promote Bone Tissue Regeneration

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Introduction: The regeneration of irregular-shaped bone defects poses enormous challenges; instructive biomaterials capable of simultaneously inducing osteogenesis and angiogenesis may hold great promise for muscklosketal tissue repair. Multifunctional scaffolds with the capability to *in situ* recruit therapeutic ions as well as bind angiogenic cues may enable an enticing avenue for tissue repair

Research design: We prepared calcium ions (Ca^{2+}) recruiting peptide-loaded poly(Lactic acid)/gelatin short fibers (PLA/G@CP) by electrospinning and homogenization. Similarly, vascular endothelial growth factor (VEGF)-binding peptide (BP) and PLA/G@CP were incorporated into gelatin methacrylate (GM) to obtain GM@BCP hydrogels.

Results and Discussion: Hydrogels loaded with the BP were shown to recruit VEGF, improve cellular growth, resolve inflammatory response, and promote angiogenesis. Whole transcriptome RNA sequencing of HUVECs further mirrored these results. On the other hand, PLA/G@CP short fiber were found to promote biomineralization via enhanced recruitment of calcium ions (Ca^{2+}). Transplantation of GM@BCP hydrogels in a rat calverial defect model facilitated bone tissue repair via concurrent osteogenesis and angiogenesis as evaluated for up to 8 weeks *in vivo* (**Fig. 1**).

Conclusion: Taken together, our approach of concurrently harnessing functional peptides for *in situ* recruitment of VEGF and calcium ions (Ca^{2+}) may provide an invaluable platform for bone tissue repair and potentially other related disciplines.

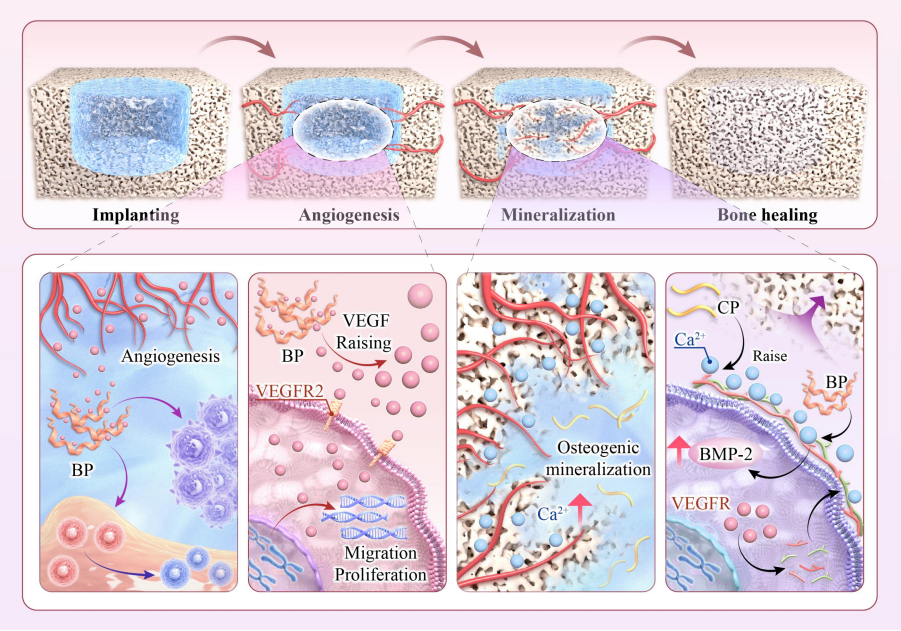

Fig. 1: Schematic illustration for the bone tissue repair with instructive scaffolds

Keywords: Peptides; Nanofiber; Hydrogel; VEGF; Bone regeneration.

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Symposia 9

Biomimetic Materials and Regenerative Medicine

Novel Applications of Cell Sheet Technology in Regenerative Medicine: from in vitro Model to Immunotherapy

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Key Words: cell sheet, extracellular matrix, *in vitro* model, immunotherapy

Introduction: Cell sheet technology (CST) is one of the well-known technologies in the field of regenerative medicine. However, traditional CST still faces challenges such as high costs and limited application scope.

Materials and methods: We developed a simple method to fabricate an off-the-shelf devitalized human fetal gingival mesenchymal stem cell sheet for burn wound healing, integrated CST with immunotherapy for tissue repair and immunotargeted therapy. As for *in vitro* applications, we reported cell sheet-based liver disease model and bone repair materials evaluation model.

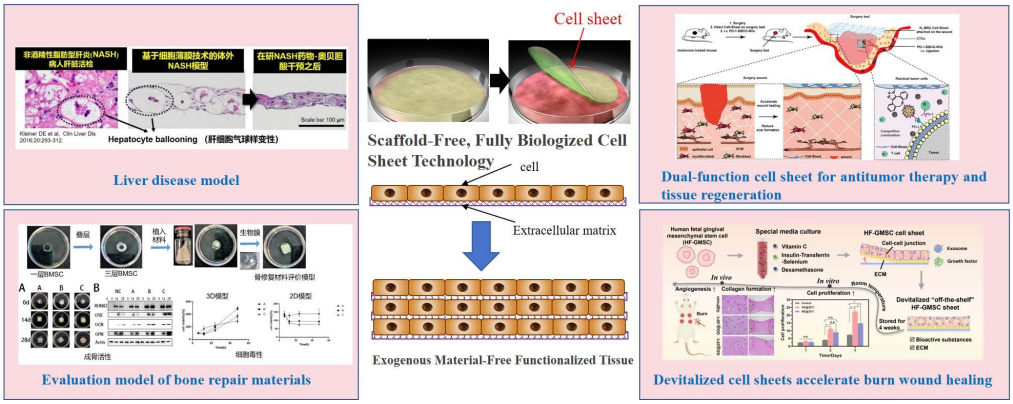
Results and Discussion:

1) Based on CST, we have developed a 3D bone defect model. Unlike 2D models, the 3D system exhibited resistance to cytotoxicity and supported long-term culture of three commercial materials. Evaluations confirmed osteogenic activity in all materials, aligning with results from animal studies.

2) Cell sheets functionalized with surface azide groups were successfully fabricated. These sheets enabled targeted enrichment of PD-1-loaded vesicles at tumor resection sites via click chemistry. Animal experiments demonstrated that the integrated therapeutic cell sheets achieved robust tissue defect repair and effectively controlled cancer recurrence and metastasis.

3) The devitalized HF-GMSC sheets stored at 25℃ demonstrated comparable efficacy to those stored at -20 ℃ and fresh sheets in the burn wound healing model. In addition, they exhibited advantages in the vascularization and regeneration of skin appendages.

Conclusion: We have expanded the applications of cell sheet technology to in vitro material evaluation models and immunotherapy and provides new insights for the development of a new generation of CST.



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Calcium Phosphate Cluster for Rapid Remineralization of Tooth Enamel

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1. Introduction

Tooth enamel remineralization is critical for repairing early-stage demineralization, yet conventional strategies face challenges in dynamic oral environments due to slow repair kinetics and stabilizers that inhibit material transformation. Rapid remineralization methods are urgently needed but require materials that balance stability during storage and responsiveness during application.

2. Research design

We synthesized ultrasmall (1–2 nm) calcium phosphate clusters (GCPC). The material's efficacy was systematically evaluated through *in vitro* tests under static and dynamic conditions, in vivo studies using female Sprague-Dawley rats, and clinical trials. Key investigations focused on GCPC's water-responsive transformation kinetics, penetration into nano-/micro-scale enamel defects, and structural/mechanical recovery of repaired enamel.

3. Main results and discussion

GCPC rapidly infiltrated enamel defects and transformed into dense hydroxyapatite (HAP) layers within 30 minutes upon water exposure. This process involved glycerol-water exchange, amorphous calcium phosphate intermediate formation, and crystallization into HAP nanorods oriented perpendicular to the enamel surface. The repaired layer restored mechanical properties (e.g., hardness, modulus) to near-native enamel levels, outperforming conventional materials requiring hours or days. Remarkably, GCPC maintained efficacy under dynamic conditions and demonstrated clinical success in restoring enamel structure and function, validated by mechanical testing and morphological analysis.

4. Conclusion

GCPC represents a breakthrough in rapid enamel remineralization, combining glycerol-enabled stability with water-triggered repair activity. Its small size, fast transformation kinetics, and compatibility with clinical workflows make it superior to existing materials. The simplicity of preparation, low cost, and proven efficacy in preclinical and clinical settings position GCPC as a scalable solution for enamel restoration, with significant potential for widespread dental applications.

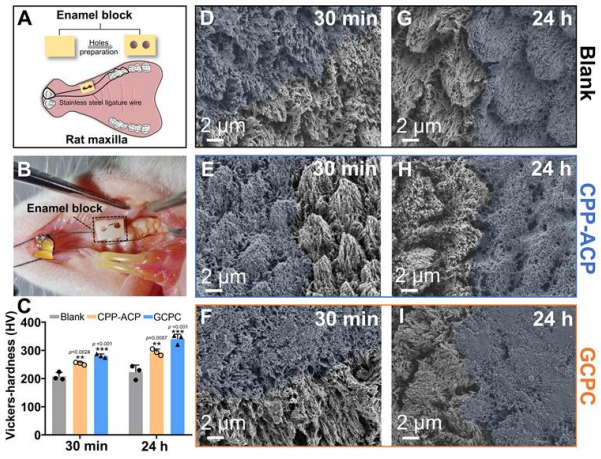

Figure 1. The repair of demineralized enamel in vivo. (A, B) Schematic (A) and photograph (B) of vivo animal model showing the etched enamel fixed in the oral cavity of rats. (C) Microhardness of the enamels repaired by different materials in vivo for 30 min and 24 h.

Key Words: Calcium Phosphate, Cluster, Remineralization, Tooth Enamel

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Biomimetic wrinkle microstructures for tissue engineering

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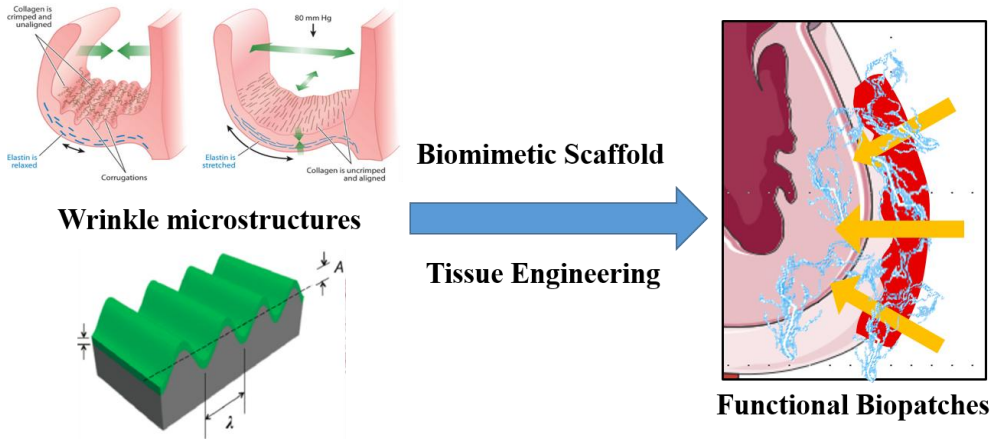
Wrinkle patterned surfaces are ubiquitous in whether in natural events or organism, endowing significant functions and thus bearing broad and fantastic applications. Due to its advantages of spontaneous nature, versatility, easy preparation in large-scale, and capability to be responsive to various stimuli, wrinkling or buckling surfaces offers a powerful alternative to prepare functional surfaces, which can tailor the encoded surface properties on demand and can find potential for wide applications in smart display, responsive microstructures, switchable wettability, smart adhesion and friction, and so on. We developed a series of dynamic wrinkled surfaces response to light, temperature, pH, and various chemicals in recent years, and explored the potential of theses microstructured surface for smart displays, memory, flexible electronics, tunable adhesion, friction, and wettability. Very recently, we present an interesting exploration of wrinkled pattern surface for regulating the behave of different tissue and stem cells such as cardiomyocytes and BMSCs and accelerating the repair of tissue injury, inspiring the new direction of functionally biomimetic bio-surfaces.



Biomimetic wrinkle microstructured scaffolds for cardiac and other tissue engineering

Key Words: biomimetic material; tissue engineering; wrinkle pattern

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Cooperative Tissue Engineering for Functional Tissue Fabrication

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Since the concept of Tissue Engineering using cells and scaffold materials was proposed by Robert Langer in 1993, various cell integration techniques have been reported. However, the technologies to date have focused on "construction of tissue structures" and have not been able to "reproduction of functional tissues" the most important aspect. This is mainly due to the fact that cells are particles with a diameter of only 15 μm, so the scaffold material is necessary for tissue structure construction. However, if the scaffold material increases, cell-cell interactions are inhibited, and cells cannot interact with each other. Conversely, when scaffold material is reduced, tissue structures cannot be formed and cell aggregates are formed, and it is difficult to construct tissues with diameters of 200~300 μm or more due to internal cell necrosis. To solve this dilemma and realize the "creation of functional tissue constructs," it was necessary to innovate with cell integration technology based on a completely new principle for compartmentalization of cells and extracellular matrix (ECM) inside 3D-tissue constructs[1], together with cell orientations.

To solve this dilemma, we discovered new concept “cooperative tissue engineering” that means cells and materials interacted each other to fabricate tissue constructs cooperatively. Nano-sized scaffolds formed on the cell surfaces induced cell-cell adhesion and integration of multiple cell types, and then the scaffolds grown to microscopic sizes, and the adhered cells on the scaffolds proliferated to cover the scaffold surfaces. The micrometer-sized grown scaffolds induced the elasticity and molecular orientation to control the cell orientation and differentiation to fabricate “functional tissue constructs”. This new concept will be powerful technology to fabricate functional tissue constructs for implantation in biomedical applications, construction of cultivated meat in food-tech application[2] and drug assessment in pharmaceutical application[3].

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Promoting Effects of Sustainably Degradable and Bioactive Magnesium Phosphate Cement in Rabbit Bone Regeneration and Screw Fixation Models

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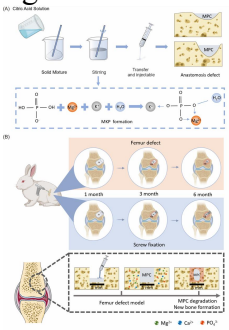
With the growing demand for orthopedic disease treatment, there is an urgent need in clinical medicine and biomaterials science to develop bone repair materials that integrate bioactivity, biodegradability, and mechanical compatibility. Traditional bone cements, such as polymethyl methacrylate (PMMA), provide short-term mechanical support but are non-degradable, bioinert, and potentially toxic. Calcium phosphate cement (CPC), on the other hand, suffers from slow degradation rates and insufficient mechanical strength. To address these limitations, this study designed a bioactive and biodegradable magnesium phosphate cement (MPC). Through in vitro and in vivo experiments, we evaluated the clinical feasibility, bioactivity, and degradation performance of MPC in bone defect repair and screw fixation. The results demonstrated that MPC not only significantly promoted new bone formation but also enhanced the initial stability of fixed screws. Furthermore, the degradation rate of MPC aligned with the growth rate of newly formed bone tissue, preventing tissue voids and ensuring continuous repair in the bone defect area. By combining controlled degradability, bioactive Mg^{2+} release, and mechanical adaptability, MPC bridges the gap between transient mechanical support and sustained biological regeneration, offering a promising solution for next-generation bone repair strategies.



Key Words: magnesium phosphate cement, bone regeneration, magnesium ion, degradable

Acknowledgements: This work was supported by the National Key R&D Program of China (2022YFE0123500), the National Natural Science Foundation of China (32201102 and 31771081), the Science and Technology Commission of Shanghai Municipality (22S31903300).

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Design of Inoganic-Organic Biommetic Scaffolds for Neurovascularized Bone Repair

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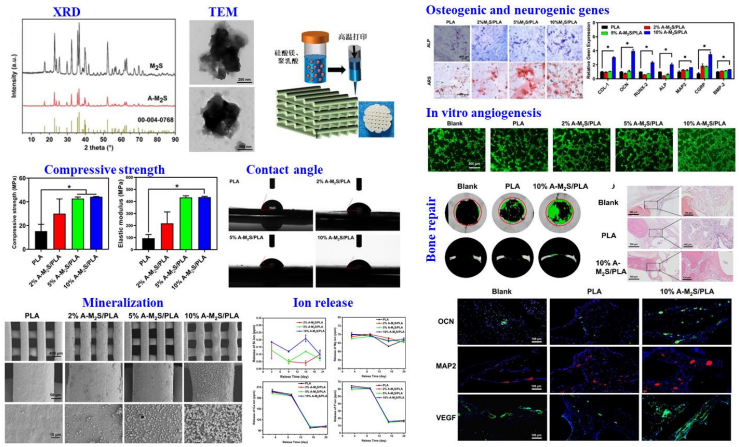
Introduction: When the osteogenesis, vascularization and neurogenesis of bone implant materials are insufficient, it is easy to lead to delayed repair and high incidence of bone nonunion [1]. Inorganic /organic composites with degradable polymers can introduce bioactive ions with the above functions, which is expected to be better applied to bone repair.

Research design: APTES modified inorganic magnesium silicate (A-M_2S) nanoparticles and organic polylactic acid (PLA) were used as matrix materials to construct A-M_2S/PLA composite scaffolds by 3D printing for neurovascularized bone repair [2].

Results and discussion: The composite scaffold has excellent mechanical properties and three-dimensional connected porous structure. With the increase of the amount of A-M_2S, the compressive strength and hydrophilicity of the scaffolds were increased, the mineralization products and the degradation rate were also increased. The composite scaffold could continuously release bioactive ions (Si^{4+} and Mg^{2+}), which promoted the osteogenic differentiation of BMSCs *in vitro*, enhanced the tube formation ability of HUVECs, and promoted the expression of genes such as NGF and CGRP in SCS. The 10% A-M_2S/PLA scaffold implanted into the critical skull defect of rats promoted new bone formation and the expression of related proteins (OCN, MAP-2 and VEGF).

Conclusion: The constructed A-M_2S/PLA has good mechanical properties and biocompatibility, which is conducive to neurovascularization and bone repair.



Key Words: Bone repair, neurovascularization, 3D printing, magnesium silicate, polylactic acid

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Durable immunomodulatory nanofiber niche for the functional remodeling of cardiovascular tissue

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Functional remodeling and prolonged anti-inflammatory responses are both vital for repairing damage in the cardiovascular system. Although these aspects have each been studied extensively alone, attempts to fabricate scaffolds that combine these effects have seen limited success. In this study, we synthesized salvianic acid A (SA, danshensu) blocked biodegradable polyurethane (PCHU-D) and enclosed it within electrospun nanofibers to synthesize a durable immunomodulatory nanofiber niche (DINN), which provided sustained SA release during inflammation. Given its excellent processability, mechanical properties, and shape memory function, we developed two variants of the DINN as vascular scaffolds and heart patches. Both these variants exhibited outstanding therapeutic effects in in vivo experiments. The DINN was expertly designed such that it gradually decomposes along with SA release, substantially facilitating cellular infiltration and tissue remodeling. Therefore, the DINN effectively inhibited the migration and chemotaxis of inflammatory cells, while also increasing the expression of angiogenic genes. As a result, it promoted the recovery of myocardial function after myocardial infarction and induced rapid reendothelialization following arterial orthotopic transplantation repair. These excellent characteristics indicate that the DINN holds great potential as a multifunctional agent for repairing cardiovascular tissue.

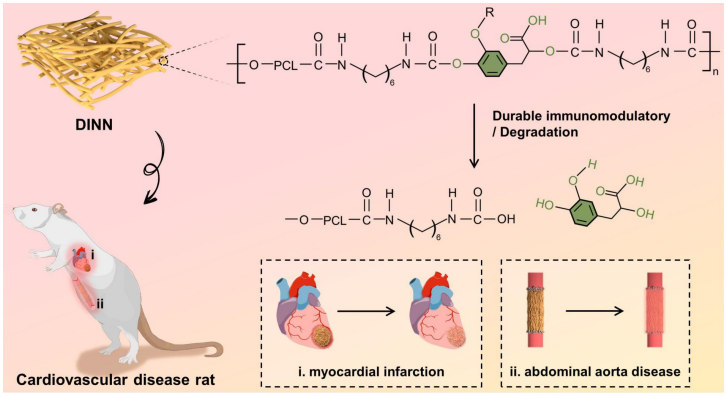

Fig. 1 The scheme of synthetic durable immunomodulatory nanofiber for the functional remodeling of cardiovascular tissue.

Key Words: inflammation; nanofiber niche; cardiovascular tissue; matrix remodeling

Acknowledgements: National Key Research and Development Program of China (2023YFC2412400, 2023YFC2412403)

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Study on the promotion of tissue regeneration by electrical stimulation in collaboration with electroactive materials

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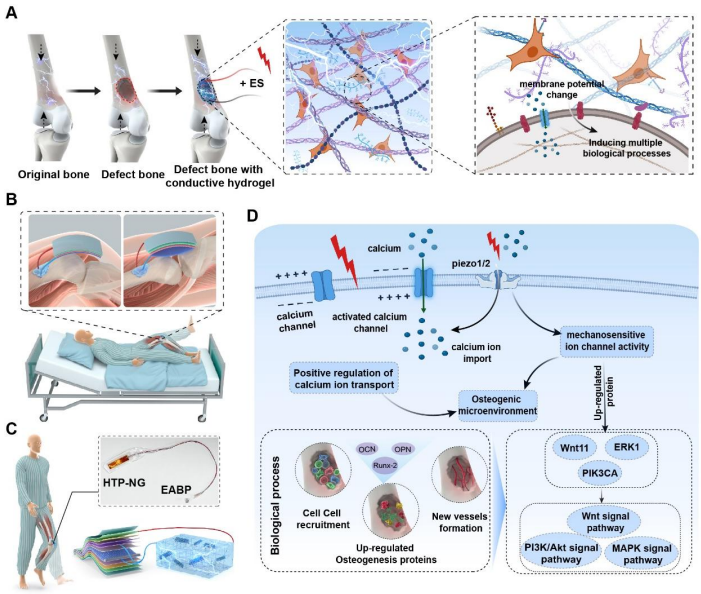
Electrical stimulation can accelerate bone-healing effectively. However, the substantial size and weight of devices result in lower patient benefits and reduced compliance. It remains a challenge to establish a flexible and lightweight implantable microelectronics stimulator for bone regeneration. Here, we use self-powered technology to realize an electric stimulator, which eliminate the weight, volume and necessary rigid packaging from circuits and battery. The fully implantable bone defect electrical stimulation (BD-ES) system combines a hybrid tribo/piezoelectric nanogenerator to provide biphasic electric pulses in response to rehabilitation exercise with a conductive bioactive hydrogel. The BD-ES system can enhance multiple osteogenesis-related biological processes including calcium ion import and osteogenic differentiation. In the rat model of critical-sized femoral defects, the bone defect has been reversed by BD-ES system, and completely healed femur within 6 weeks. This work is expected to advance the development of symbiotic electrical stimulation therapy devices without batteries and circuits.



Key Words: Electrical stimulation; nanogenerator; biphasic electric pulses; bone defects

Acknowledgements: This work was supported by the National Natural Science Foundation of China (31771081, 52202108), the National Key R&D Program of China Grants (2022YFe0123500), the Science and Technology Commission of Shanghai Municipality (22S31903300), and the Fund of Shanghai Stomatological Hospital (SSH-2024-C01, SSH-2024-A01, SSH-2024-B02, SSH-2024-B06).

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Chemically Modified miRNA Delivery via DNA Tetrahedral Nanostructures Enhances Angiogenesis and Dental Pulp Regeneration

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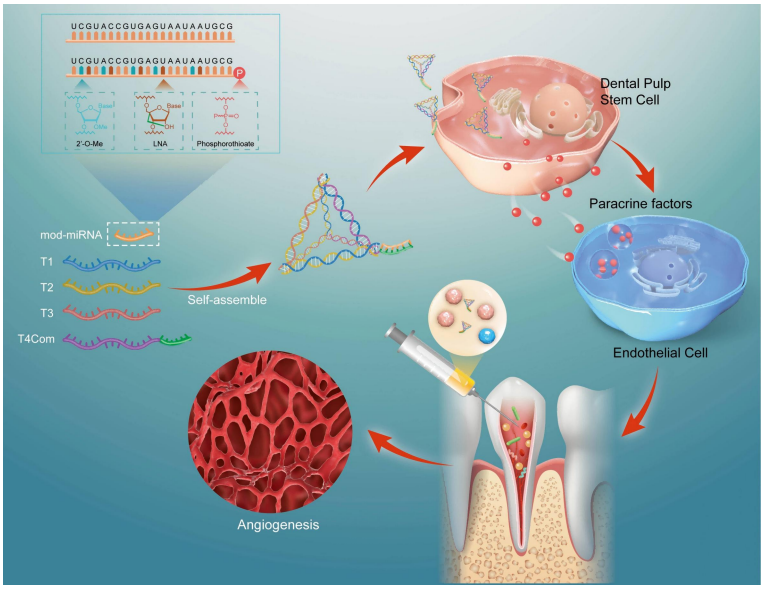
Abstract

Dental pulp regeneration holds promise for restoring tooth vitality, but achieving functional angiogenesis remains challenging. We developed a DNA tetrahedral nanostructure (TDN) platform delivering chemically modified miR-126-3p (miR@TDNs) to enhance angiogenic activity in dental pulp stem cells (DPSCs). Modifications such as 2'-O-methyl, 2'-fluoro, and LNA improved miRNA stability and cellular uptake efficiency . miR@TDNs promoted DPSC proliferation, migration, and angiogenic gene expression in vitro, and enhanced endothelial tube formation through indirect paracrine signaling mechanisms. In vivo, miR@TDNs significantly accelerated vascular network formation and promoted the regeneration of pulp-like tissues, transcriptome analysis revealed activation of PI3K-Akt and cell cycle pathways. These findings suggest that miR@TDNs are a potent gene delivery strategy for the advancement of vascularized dental pulp regeneration.



Key Words: Dental pulp regeneration, Angiogenesis, DNA tetrahedral nanostructure, miR-126-3p, Stem cell therapy

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Bioorthogonal targeted cell membrane vesicles/cell-sheet composites reduce postoperative tumor recurrence and scar formation of melanoma

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Introduction: While surgical resection is the predominant clinical strategy in the treatment of melanoma, postoperative recurrence and undetectable metastasis are both pernicious drawbacks to this otherwise highly successful approach. Furthermore, the deep cavities result from tumor excision can leave long lasting wounds which are slow to heal and often leave visible scars. These unmet needs are addressed in the present work through the use of a multidimensional strategy, and also promotes wound healing and scar reduction. Herein MSC cell sheet surfaces were modified with azide (N_3) group and then attached on the wound without suture. Subsequently, PD-1 NVs decorated with the complementary DBCO were injected intravenously. Through the bioorthogonal reaction, PD-1 NVs were accumulated to prevent tumor recurrence in situ by re-activating T cells.

Method: In the first phase, cell membrane-derived nanovesicles (NVs) are engineered to show PD-1 and dibenzocyclooctyne (DBCO). The activation of T cells were verified *in vivo* and *in vitr*o. In the second phase, N_3 labeled MSCs were cultured into cell sheets and then the repair ability was verified. Nextly, the biological orthogonal reaction between DBCO group and N_3 group was verified *in vivo* and *in vitro.* Lastly, postoperative recurrence model and lung metastasis model were built to systematically evaluate *in vivo* therapeutic effects.

Results and discussion: (1) PD-1-DBCO NVs could activate T cells, reduce depletion, and enhance tumor lethality. (2) After N_3 labeled, MSCs still could promote the proliferation and migration of fibroblasts. (3) Biological orthogonal reaction can achieve targeting *in vivo* and *in vitro*. (4) In the postoperative recurrence model, the combined treatment system of could significantly improve the immune microenvironment to inhibit the growth of melanoma, as well as promoting wound healing and reducing scar formation. (5) In the lung metastasis model, PD-1-DBCO-NVs could reduce the formation of metastases.

Conclusion: This strategy can inhibit postoperative tumor recurrence and metastasis, whilst also promoting wound healing and reducing scar formation. It provided a new idea for more functional modification and multi-dimensional combined application of Cell Sheet.

Key Words: bioorthogonal chemistry, MSC Cell Sheet，postoperative treatment of melanoma

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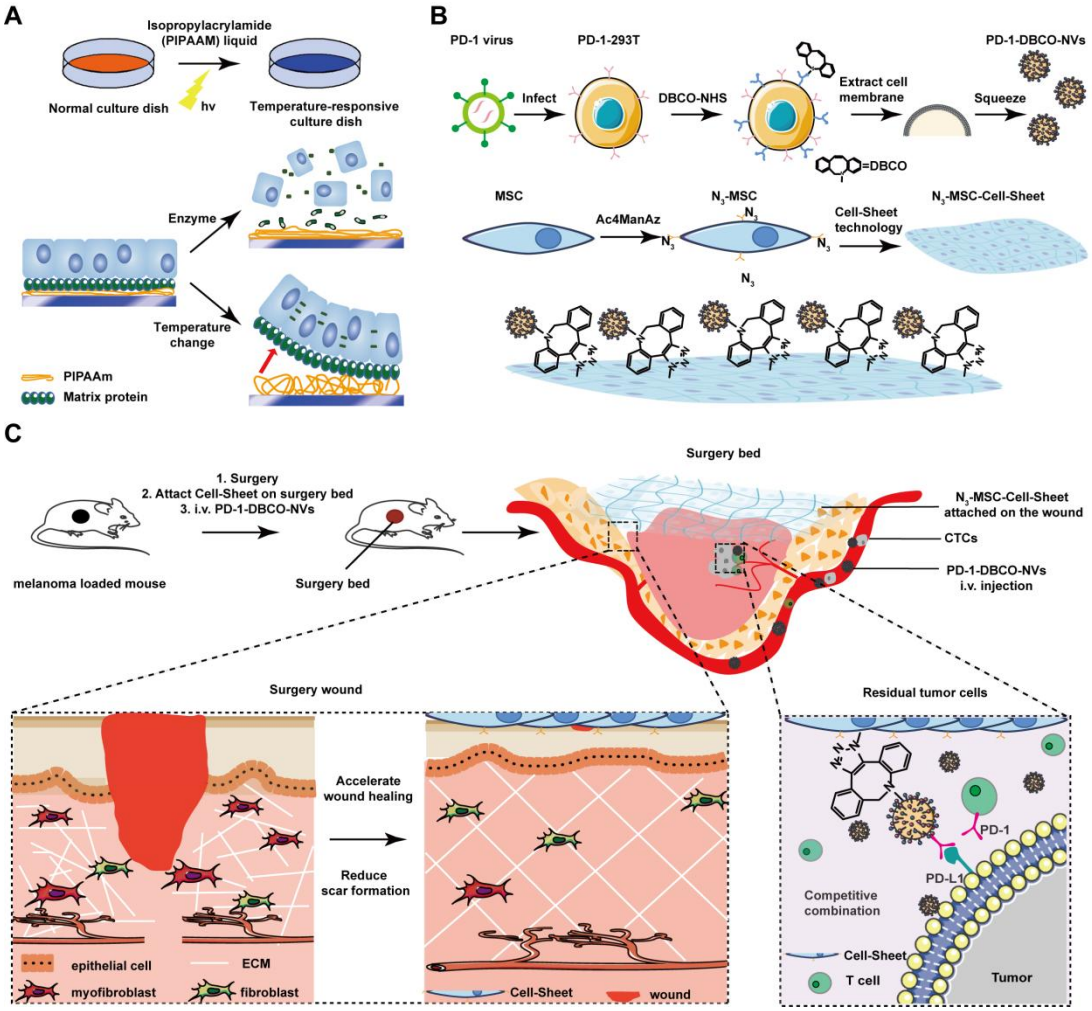

Symposia 10

Biopolymer Synthesis

From Fats to Bone: Applications for Oral & Maxillofacial Regeneration

Bee Tin Goh

Currently, autogenous bone is considered the gold standard as a graft material for reconstruction of bone defects. This implies that the patient is subjected to additional surgery and its associated morbidities and expenses. Allografts and xenografts are alternatives, but they have unpredictable results and subject the patient to risks of disease transmission and adverse immune reactions. Bone regeneration using tissue engineering principles holds promise to obviate these shortcomings. Our team at the National Dental Research Institute Singapore has been collaborating with bioengineers and material scientists to develop novel devices and innovative approaches to bone regeneration for application in the oral and maxillofacial region. The techniques are kept simple, minimally invasive and relatively inexpensive so they may be easily adopted in clinical practice. This presentation will share preclinical studies on the use of adipose-derived mesenchymal stem cells extracted and implanted at the time of the primary surgery for bone regeneration.

Fluidic Membrane-Bound Protocells (FMPs): An Adaptive Platform for Next-Generation Intelligent Medicine

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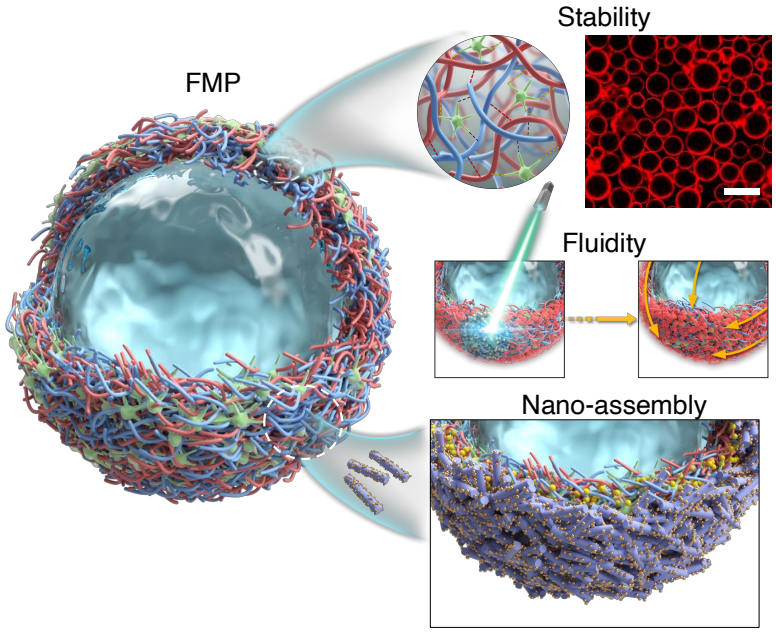
The development of membrane-encapsulated protocells capable of facilitating sequential biochemical reactions within distinct micro-compartments marks a significant advancement in soft matter systems[1]. However, many artificially designed protocells that mimic cellular compartments are often unstable or prone to rupture in biological environments, and their limited post-functionalization capacity constrains their biomedical applications[2]. In this study, we explore the phase separation of tannic acid (TA) and polyethylene glycol (PEG) to generate coacervate droplets. Upon the introduction of polyvinylpyrrolidone (PVP), a dense hydrogen-bonding network spontaneously forms at the droplet interface, giving rise to highly stable fluidic membrane-bound protocells (FMPs)[3]. These FMPs can be readily functionalized by integrating nanomaterials via electrostatic interactions, enabling the construction of cascade reactions for biomedical purposes. As a demonstration, we assemble nanozymes (Pt/CeO_2) onto Fe^{3+}-stabilized FMPs to create $Pt/CeO_2@Fe^{3+}$/FMPs, which efficiently catalyze the degradation of uric acid and its toxic byproduct, H_2O_2, offering a promising approach for precision gout treatment.



Key Words: Protocell, Microfluidic assembly, Intelligent medicine, Coacervate droplets, Catalysis

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Developing "Phormulations" for Phages

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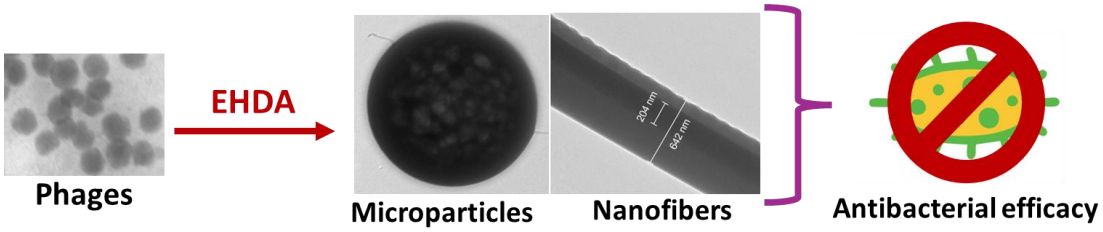
Bacterial infections contribute to millions of deaths (7.7M in 2019). The most common medical intervention to combat these is the use of antibiotics. However, the emergence of multi-drug-resistant bacteria is a significant and growing threat associated with *ca.* 4.95M deaths in 2019 [1]. *Pseudomonas 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.



Key Words: electrospinning, electrospraying, bacteriophages, antibiotic resistance.

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A novel ligand-modified nanocomposite microparticles improved efficiency of quercetin and paclitaxel delivery in the non-small cell lung cancer

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Abstract:

Non-small cell lung cancer (NSCLC), a prevalent global malignancy, faces therapeutic limitations due to paclitaxel (PTX) resistance and systemic toxicity. This study addresses these challenges by developing cetuximab (Cet)-modified PTX/quercetin (QUE)-loaded nano-composite microparticles (P/Q@CNMPs). PTX efficacy is hindered by ATPase-mediated hydrolysis and P-glycoprotein (P-gp)-driven drug efflux. QUE counteracts resistance via non-competitive ATPase inhibition and P-gp blockade[1]. Concurrently, epidermal growth factor receptor (EGFR)-targeting Cet enhances tumor specificity by binding EGFR-overexpressing NSCLC cells, minimizing off-target toxicity. The pulmonary drug delivery system (PDDS) leverages 1-5 μm microparticles for optimal lung deposition, overcoming nanoparticle exhalation limitations[2]. These microparticles release PTX/QUE-loaded nanoparticles (NPs) post-deposition, microparticles ensure lung retention, while NPs improve cellular uptake. This design integrates micro-nano advantages, enhancing drug bioavailability. QUE-mediated resistance reversal synergizes with Cet-driven EGFR targeting.Microparticles (1-5 μm) enable inhalable aerosol delivery, transitioning to tumor-penetrating NPs (<200 nm) post-deposition. Co-loading PTX (low solubility) with QUE improves chemotherapeutic applicability.

The Cet modification on the PTX/QUE-loaded nano-composite microparticles (P/Q@CNMPs) to obtain an active targeted delivery system, playing a role in the NSCLC of EGFR high expression. This drug delivery system was expected to enhance the accuracy therapeutic effect to the positive expression EGFR NSCLC cells, reduce the toxicity on other major organs, and improve the application of the low solubility chemotherapy drugs.

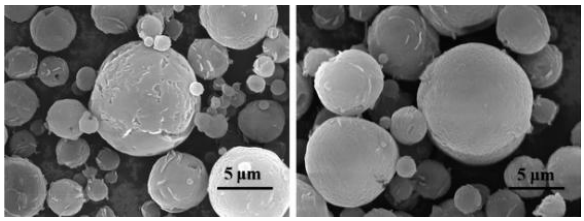

Figure.1 SEM microphotographs of P/Q@NMPs (A)

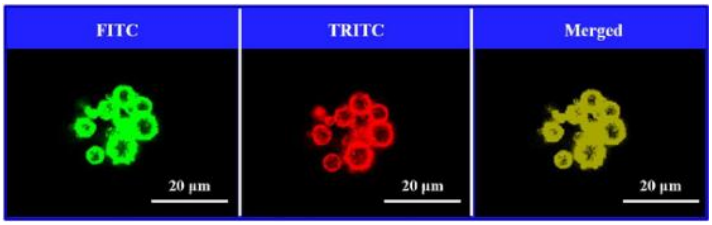

Figure.2 Colocalization of TRITC-labeled PCNP and FITC-labeled QCNP in P/Q@CNMPs by confocal laser scanning microscopy (CLSM). The scale bar is 20 μm.

Keywords: Microspheres; Pulmonary drug delivery system; NSCLC.

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Acknowledgments: The authors are grateful for the generous financial support from National Natural Science Foundation of China (No.81973671); Project of Collaborative Innovation Center for Target Drug Delivery System of Weifang Medical University (2017).

Procyanidin-crosslinked gradient silk fibroin composite nanofiber scaffold with sandwich structure for rotator cuff repair

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Improving the regeneration of the tendon-bone interface (TBI) helps to decrease the risk of rotator cuff retears after repair surgeries. Unfortunately, the lack of inherent healing capacity of the TBI, insufficient mechanical properties, and abnormal and persistent inflammation during repair are the key factors leading to suboptimal healing of the rotator cuff. Therefore, a high-strength rotator cuff repair material capable of regulating the unbalanced immune response and enhancing the regeneration of the TBI is urgently needed. In this study, a novel sandwiched silk fibroin composite nanofiber scaffold with a biomimetic gradient structure was prepared through layer-by-layer continuous electrospinning, and then procyanidin was utilized to further enhance the mechanical properties and biological activities of the scaffold.The physicochemical characterization revealed that the procyanidin-crosslinked sandwiched gradient scaffold (GMPC) possessed an appropriate porosity and pore size and superior mechanical properties. Cytocompatibility assessment and immunofluorescence staining indicated that GMPC allowed rapid adhesion, proliferation, and infiltration of osteoblasts. ELISA and macrophage polar ization experiments further confirmed that GMPC could effectively inhibit excessive inflammation in injured tissues and regulate the polarization of macrophages to the beneficial phenotype. Therefore, the procyanidin crosslinked sandwiched gradient nanofiber scaffold might be a promising candidate for rotator cuff repair.

Key Words: Rotator cuff, Electrospinning, Procyanidin, Polyethylene terephthalate, Inflammation

Acknowledgements:

This study was supported by the Chenguang Program of Shanghai Education Development Foundation and Shanghai Municipal Education Commission (23CGB08), School-level Project of Shanghai Zhongqiao Vocational and Technical University (ZQZR202433), Project of Shanghai Science and Technology Commission (20Y11913300), Con struction Project of Shanghai Engineering Technology Research Center (20DZ2255900), Project of Shanghai Pudong New Area Municipal Health Commission (PW2022D-11), and Project of Shenkang Hospital Development Center of Shanghai (SHDC12020118).

A novel biodegradable elastomer with anticoagulant and antiplatelet properties for vascular tissue engineering

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In clinical practice, high-effective antithrombosis remains a challenge for blood-contacting medical devices. Inspired by the enhanced antithrombogenicity of anticoagulant and antiplatelet combination therapy[1], a strategy is proposed to synthesize dual-pathway antithrombotic polymers by incorporating anticoagulant and antiplatelet dual functional groups into a single thermosetting polymer chain. The synthesized polymer shows increased antithrombogenicity in vitro, with prolonged activated partial thromboplastin time (APTT) and decreased platelet adhesion. Additionally, it downregulates the expression of coagulation- and inflammation-related factors in rabbit plasma after *ex vivo* arteriovenous shunt assay and maintains patency of small vascular grafts for at least 6 months without thrombosis on the luminal surface after *in vivo* replacement of rabbit carotid artery. This work provides a new approach to producing novel antithrombotic polymers for vascular tissue engineering.

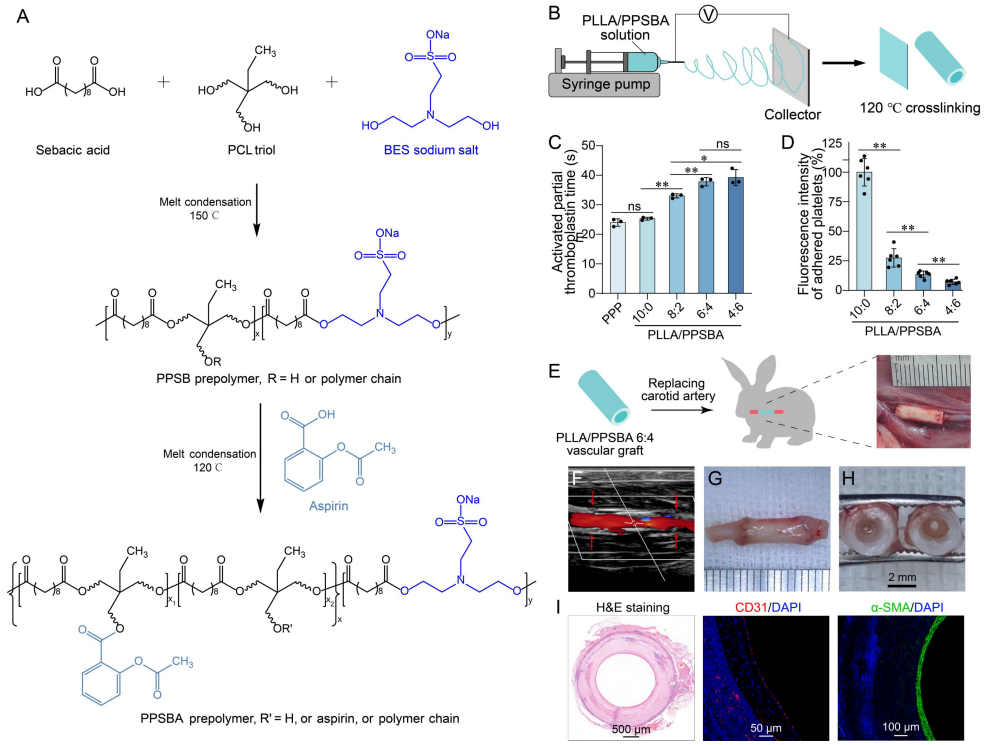

Figure. Schematic representation of (A) the synthesis of dual-pathway antithrombotic PPSBA prepolymer and (B) the fabrication of PLLA/PPSBA composite scaffolds. The (C) anticoagulant and (D) antiplatelet properties of PLLA/PPSBA scaffolds. (E) Schematic representation of replacing the rabbit carotid artery with PLLA/PPSBA vascular graft. (F) Color Doppler ultrasonography images of vascular graft after transplantation for 3 months. The (G) gross, (H) cross-sectional views, and (I) H&E and immunofluorescent staining for CD31 and α-SMA of harvested vascular grafts after transplantation for 3 months.

Key Words: dual-pathway antithrombogenicity, anticoagulant, antiplatelet, sulfonic groups, aspirin

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Glucose-Responsive Self-Healing Hydrogels Promote Diabetic Wound Healing

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[**Introduction**] Hyperglycemic environment, bacterial infection and inflammatory reaction will cause serious secondary damage and hinder wound healing. Preparation of glucose-responsive hydrogels with hypoglycemic, antibacterial and anti-inflammatory properties is an important strategy to promote wound healing in diabetes. [**Research design**] Self-healing hydrogels with glucose responsiveness were prepared by Schiff base reaction and the introduction of borate ester bond. Specifically, hyaluronic acid is oxidized to oxidized hyaluronic acid, and oxidized hyaluronic acid grafted 3-aminophenylboronic acid reacts with carboxymethyl chitosan to generate oxidized hyaluronic acid 3-aminophenylboronic acid carboxymethyl chitosan hydrogel, in which berberine is loaded (named OAPCS-BH hydrogel). [**Results**] OAPCS-BH hydrogel showed a sensitive glucose response when the borate bond was broken and berberine was released under the hyperglycemic environment. Berberine and carboxymethyl chitosan were jointly antibacterial. OAPCS-BH had good biocompatibility, antibacterial, anti-inflammatory and antioxidant properties, and could effectively promote the wound healing of diabetes. [**Conclusion**] In general, glucose responsive hydrogel has potential application value in the process of rapid and continuous drug release, and is a good choice for promoting wound healing in diabetes.

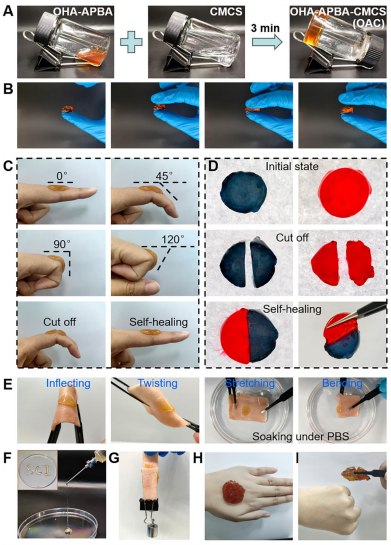

Figure1. Characterization of the Physicochemical Properties of the Hydrogel. A. Gelation time of the hydrogel. B. Elasticity characterization of the hydrogel. C. Finger adhesion property of the hydrogel. D. Self-healing performance of the hydrogel. E. Pigskin adhesion property of the hydrogel. F. Injectability of the hydrogel. G. Maximum weight that hydrogel can bear when adhering to pig Pigskin H. Hand adhesion of hydrogel. I. Cleanability of hydrogel on the back of the hand.

Key Words: Hydrogel, Glucose responsiveness, Berberine, Antibacterial, Diabetic wounds.

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Boron-Doped Silica/Chitosan-based Elastic Three-dimensional Sponge Scaffold for Bone Regeneration

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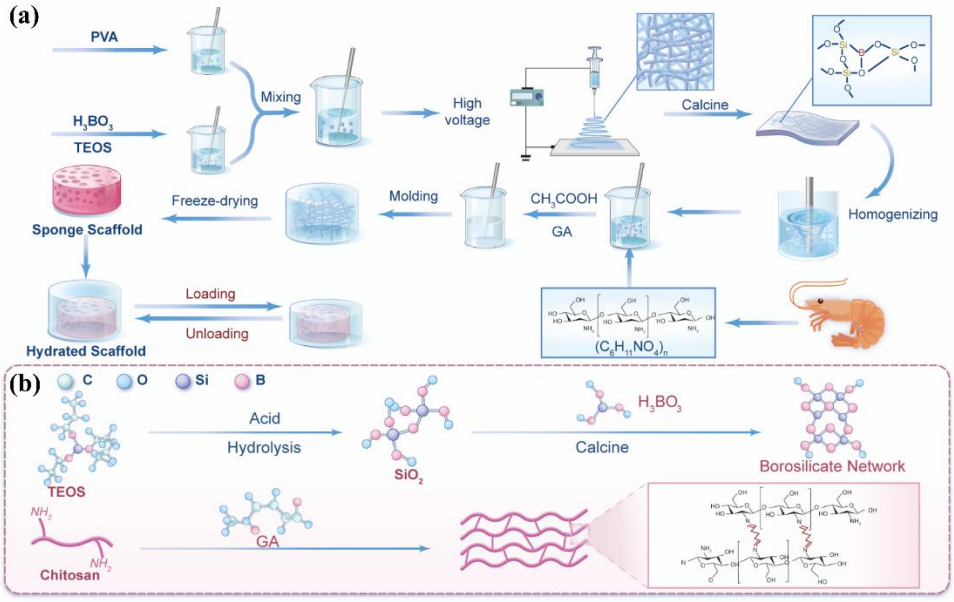
Bone regeneration is crucial for repairing irregular bone defects, restoring skeletal structure and function, and promoting healing following injury. Sponge scaffolds, characterized by their high porosity and mechanical strength, are considered as effective biomaterials for bone tissue repair. In this study, we fabricated flexible silica (SiO_2) nanofiber membranes using electrospinning, which contained different concentrations of boron ions (B^{3+}). These SiO_2 fibers further combined with chitosan (CS) to create three-dimensional (3D) sponge scaffolds. Scaffolds exhibited remarkable elastic memory in the hydrated state, thereby enabling them to conform perfectly to irregular bone defects upon implantation. Scaffold containing lower concentrations of boron ions (B^{3+}) (CS/SiO_2-B1), selected through *in vitro* assays, could synergistically release boron and silicon ions and promote the proliferation and migration of cells related to bone regeneration. CS/SiO_2-B1 scaffolds also showed significantly higher expression of angiogenesis- and osteogenesis-related genes *in vitro*. In a rat cranial defect model, CS/SiO_2-B1 scaffolds promoted *de novo* bone production 6 weeks post-implantation. Taken together, these 3D sponge scaffolds may have broad implications for bone tissue repair and potentially other bio-related disciplines.



Key Words:c Sponge; Chitosan; Short silica nanofiber; Electrospinning; Bone regeneration

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Symposia 11

Cell Biology

Protective effect of berberine on cochlear hair cell injury induced by neomycin

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Abstract

Neomycin is commonly used clinically to treat infections caused by Gram-negative bacteria. Although they are the most widely-used antibiotics due to their high efficacy and low cost, several main adverse effects have been reported including nephrotoxicity and ototoxicity. Its use can cause severe and permanent hearing loss. The hair cells of mammalian cells are non-regenerative, so overcoming the hair cell damage caused by neomycin is essential for hearing protection. Berberine (BBR) is a bioactive compound found in medicinal plants that is known to have anti-inflammatory and antibacterial effects. To determine protective effect of berberine in neomycin-induced ototoxicity using corti explants from mouse. Cytoplasmic ROS levels were analyzed, and TUNEL assay was performed to detect apoptosis signals, The expression of apoptosis-related genes was analyzed by qPCR. As the results, it was found that BBR significantly prevented neomycin-induced hair cell loss by inhibiting excessive accumulation of cytoplasmic ROS. Furthermore, BBR down-regulated the expression of apoptotic gene and up-regulated the expression of anti-apoptotic gene.It eventually inhibited DNA fragmentation. In summary, all results suggest that BBR has potential as a new and effective oto-protective agent, operating via the PI3K/AKT signaling pathway.

Keyword: Neomycin, Ototoxicity, Berberine, Hair cells

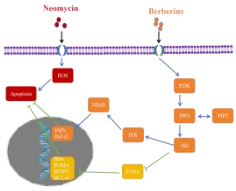

Fig. 1. Schematic diagram of protective mechanism of BBR against neomycin-induced hair cells damage. NM inhibits the PI3K-AKT signaling pathway, thereby inducing cell apoptosis. BBR inhibits apoptosis through the PTEN Akt signaling pathway.

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Symposia 12

Decellularized Tissue

Inflammation-modulating elastic decellularized extracellular matrix scaffold promotes meniscus regeneration

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Introduction: The meniscus plays a vital role in maintaining proper knee function**.** Its ability to repair itself after injury is limited due to the lack of blood vessels. Traditional treatments such as meniscectomy, although widely used, may increase the risk of osteoarthritis. Currently, meniscal decellularized matrix (dmECM)-derived scaffolds have attracted much attention in meniscal repair due to the tissue-specific bioactivity and bionic structure. However, the practical application of dmECM is constrained by foreign body response (FBR), and there is a need to focus on the modulation of inflammation and the development of smart biomaterials that modulate the immune microenvironment.

Research design: Porcine meniscus was pulverized by cyclic freeze-thaw grinding and then treated with DNase to obtain fine dmECM particles. Followed by lyophilization and crosslinked by dehydrothermal treatment, the porous precursor dmECM scaffolds were obtained. Copolymers of CS and IBU were prepared by EDC/NHS and grafted onto the dmECM surface by amination reaction to produce dmECM/CS-IBU scaffolds[1].

Results & Discussion: The dmECM/CS-IBU scaffolds had a porous structure, comparable mechanical strength and elastic properties. The scaffolds promoted chondrocyte proliferation and retained chondrogenic properties. In addition, the scaffolds had significant anti-inflammatory effects and synergized with antioxidants. In *in vivo* subcutaneous experiments, neutrophils were distributed only in the center of the scaffolds, while pro-repair pan-macrophages were enriched in the edge region, suggesting that the scaffolds could accelerate tissue regeneration by modulating the inflammatory microenvironment. In a partial rabbit meniscal defect model, the dmECM/CS-IBU scaffold promoted chondrocyte-like cell proliferation and ECM secretion, and optimized the spatial distribution of type I/II collagen, indicating the promotion of *in situ* meniscus repair.

Conclusion: This study provides a feasible strategy for fabricating scaffolds with tissue-specific bioactivity and inflammation-modulating ability that can synergistically promote meniscal repair and regeneration. Inflammation-modulating meniscal scaffolds have potential applications in promoting the repair of meniscus white zone injuries and could be an effective alternative to conventional meniscus repair methods.

Key Words: cyclic freeze-thaw grinding, decellularization, extracellular matrix, meniscus, scaffolds

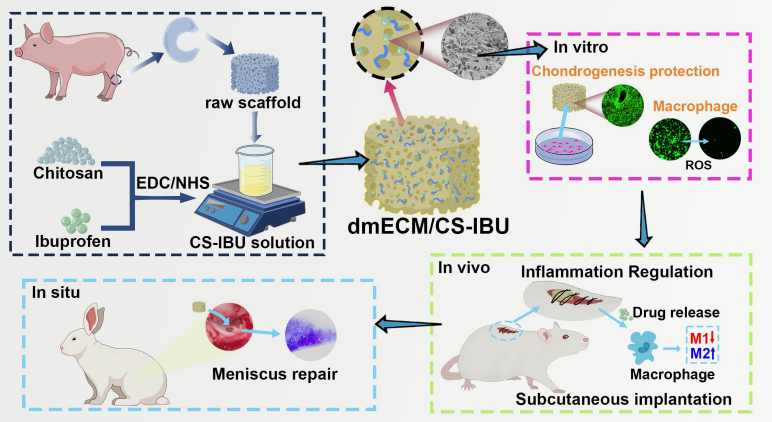

Figure 1 Preparation process of dmECM/CS-IBU scaffolds.

References

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Symposia 13

Drug Delivery Systems

Spatiotemporal Sequential Chidamide Delivery Regulates Macrophage Reprogramming in Response to the Tumor Microenvironment through HDACs-STAT3 in the Progression of Lymphoma

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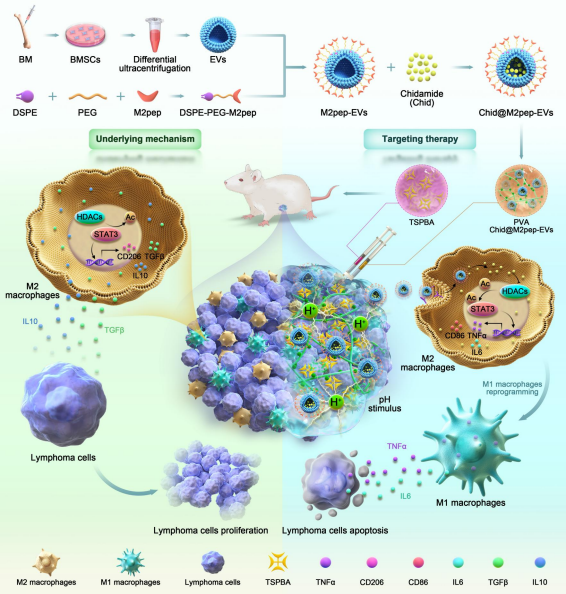
B-cell lymphoma accounts for 85%-90% of all non-Hodgkin lymphoma cases, and M2 macrophages play a role in promoting lymphoma cell proliferation and migration within the tumor microenvironment. Despite receiving standard clinical chemotherapy, 30%-40% of patients experience relapse, and typically have a poor prognosis. This study found that the presence of M2 phenotype macrophages in the microenvironment of B lymphoma patients is due to the deacetylation of STAT3 induced by histone deacetylases (HDACs). Chidamide (Chid), a broad-spectrum HDAC inhibitor, has tumor-suppressive effects at high doses and immune-modulating effects at low doses. The current clinical applications of Chid predominantly focus on its tumor-suppressive effects at high doses, which are often accompanied by significant adverse events. To address this, on the basis of the acidic microenvironment of lymphoma, we developed a targeted drug delivery system using M2-targeting peptide-modified extracellular vesicles (M2pep-EVs) to deliver Chid. Then, a pH-responsive hydrogel was formed from TSPBA and PVA in respond to the acidic microenvironment. After the hydrogel was formed in situ in the lymphoma, M2pep-EVs loaded with Chid were released in a responsive manner. Upon uptake by M2 macrophages, Chid inhibits the function of HDACs and enhances STAT3 acetylation. This results in a reduction in the proportion of M2 macrophages and the reprogramming of macrophages into M1 macrophages. M1 macrophages secrete inflammatory cytokines, which kill lymphoma cells and promote their apoptosis, thus achieving therapeutic effects on B-cell lymphoma. Overall, we utilized M2pep-EVs combined with pH-responsive hydrogels, which exhibit excellent condition-responsive properties and M2 macrophage-targeted delivery of Chid, reducing the dosage needed to mitigate adverse events. Our study proposes a promising strategy for the clinical treatment of B-cell lymphoma.

Key Words: Chidamide, lymphoma, engineered EVs, hydrogel, macrophage reprogramming



PSA(pressure-sensitive adhesive) Transdermal Patch by Way of Melt Electrospinning: Fabrication and Performance

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Melt-electrospun drug-loaded fibers exhibit unique advantages in controlled drug release. This study innovatively prepared tandospirone and progesterone-loaded styrene-isoprene-styrene (SIS) PSA fiber patches using melt electrospinning technology, systematically comparing their performance with conventional coating patches. Experimental results demonstrated that the fibrous structure effectively suppressed initial drug burst release while enhancing terminal release rate. Pharmacokinetic data revealed that the fiber patches achieved 1.79-fold higher bioavailability compared with oral administration and maintained stable blood drug concentration over extended periods. The developed patches simultaneously exhibited excellent adhesion (> 7 day) and breathability(only 37.06 Pa), providing both theoretical foundation and technical solutions for novel transdermal drug delivery systems.

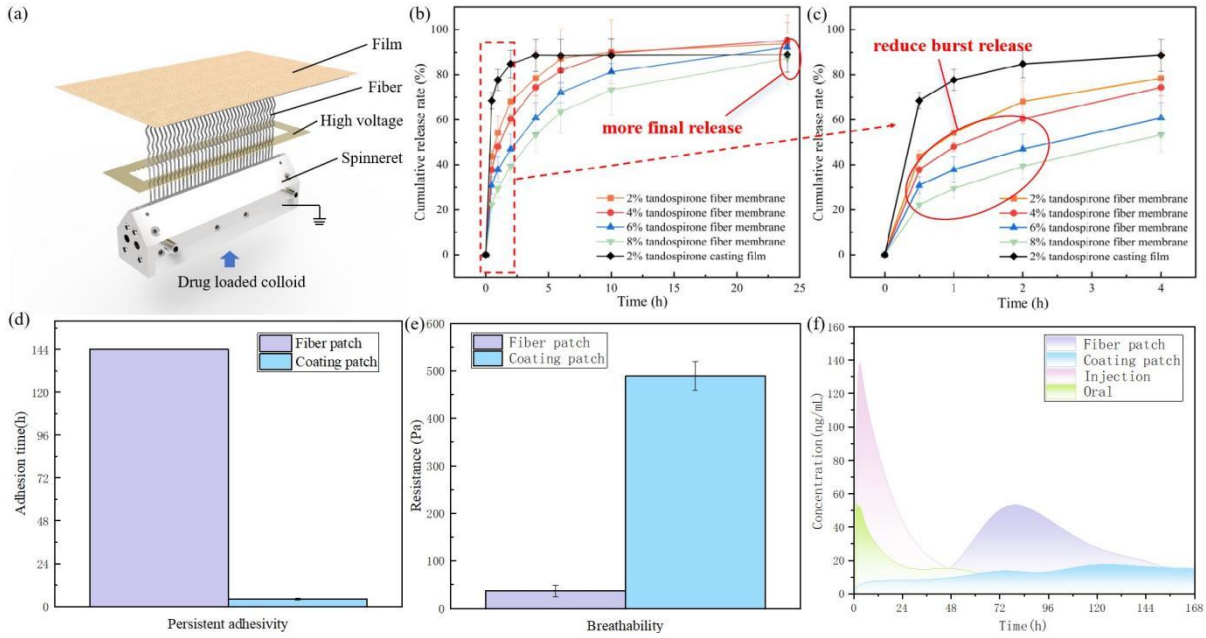

Figure 1: (a) PSA transdermal patch by way of melt differential electrospinning; (b) and (c) Cumulative release results; (d) Persistent adhesivity of patchs; (e) Breathability of patches; (f) Pharmacokinetic results.

Key Words: melt electrospinning, control release, drug delivery, drug-loaded fibers

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Peptide dendritic polymers-based nanomedicines for cancer therapy

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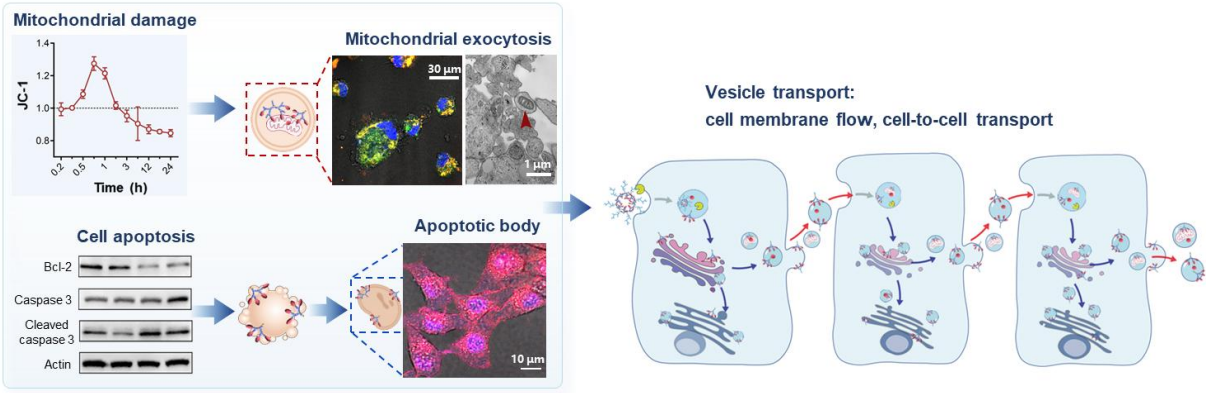
The dense extracellular matrix in solid tumors, particularly in triple-negative breast cancer (TNBC), impedes drug penetration and reduces therapeutic efficacy. To address this, our group has developed peptide-based dendritic polymers that enhance drug penetration via vesicle transport. Upon entering TNBC tumor tissue, these polymers undergo enzyme-sensitive degradation of short peptides by cathepsin B. This releases the drug and its conjugated dendritic fragments, which bind efficiently to cell membrane lipids and incorporate into membrane-bound organelles like the Golgi apparatus and endoplasmic reticulum, forming micro-vesicles. This process generates active membrane flow, facilitating intercellular drug transport and achieving deep penetration into tumors larger than 200 mm^3. Moreover, the drug and its conjugated materials disrupt mitochondrial homeostasis, stimulating mitochondrial exocytosis and forming vesicles that encapsulate mitochondria and carry the drug. This vesicle transport further enhances drug penetration within the tumor. Additionally, the sustained-release drug and its conjugated fragments induce apoptosis, forming drug-loaded apoptotic bodies that are taken up by neighboring cells through vesicle transport, facilitating deep penetration into the tumor tissue. In summary, unlike passive diffusion of free drugs and traditional delivery systems, peptide-based dendritic polymers actively promote drug penetration in TNBC through vesicle transport, achieving more effective drug delivery within the tumor.



Abstract graphic: Peptide dendritic polymers-based nanomedicines actively promote drug penetration in TNBC through vesicle transport.

Key Words: Peptide Dendritic Polymer, Drug Delivery, Drug Penetration, Vesicle Transport

Acknowledgements: This work was financially supported by the National Natural Science Foundation of China (32271445).

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Responsive Release of Nucleic Acid Drugs for Precision Tumor Therapy

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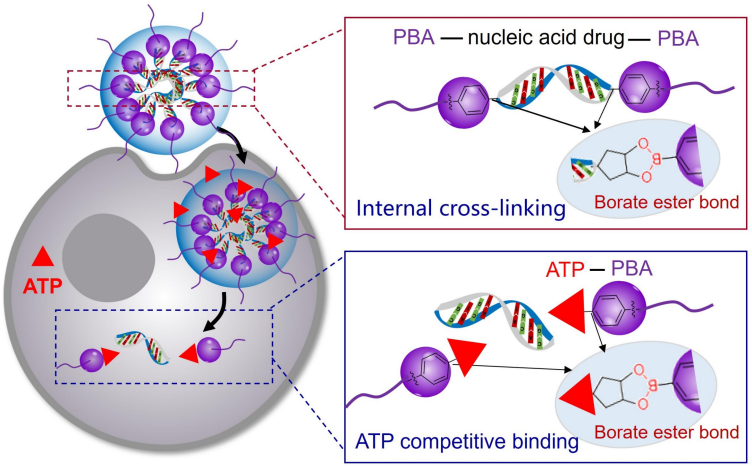
Nucleic acid-based therapy is a milestone in the history of drug development. Nevertheless, their degradation problems in vivo and poor endosomal escape are challenges that need to be addressed. Here, we designed an adenosine triphosphate (ATP)-activated self-assembled drug of phenylboronic acid (PBA) and nucleic acid drug (PBANA), which was formed by esterification and cross-linking between the boronic acid ligand of PBA and the hydroxyl group of nucleic acid. The unique chemical structure of PBA allows it to combine with cis-diols to form reversible borate bonds. In the tumor cytoplasm, high concentrations of ATP can competitively react with PBANA drugs, leading to the formation of a more stable PBA-ATP complex that facilitates the release of nucleic acid drugs. The findings indicated that PBANA drugs induced higher endosomal escape efficiency and demonstrated significant gene silencing effects in tumor cells. Additionally, PBANA drugs have excellent anti-tumor effects and good biocompatibility *in vivo*. In conclusion, our research presents a versatile and effective strategy for the delivery of nucleic acid drug, enabling responsive release through PBA modification for precise and efficient antitumor therapy.



Key Words: Nucleic acid drugs, PBA, ATP response, precise therapy

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pH-responsive Dissociable Liposome/Ferritin Nanoparticles for Treating Acute Epilepsy through Regulating Microvascular Stabilization and Remodeling Inflammatory Microenvironment

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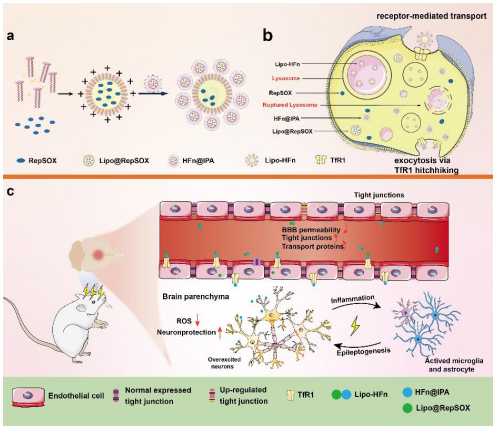
Introduction: Epilepsy is a complex central nervous system disorder. Although the exact etiology remains incompletely understood, evidence suggests that dysfunction of the blood brain barrier (BBB) and inflammatory responses in foci significantly contribute to the exacerbation of epilepsy. Targeting and crossing the BBB effectively while interrupting the vicious cycle of epileptic development pose major challenges in epilepsy treatment.

Research design: We design a dual-functional system, Lipo-HFn, comprising RepSOX-loaded liposome (Lipo@RepSOX) and indolepropionic acid (IPA)-loaded heavy ferritin (HFn) (HFn@IPA), through a simple electrostatic complexation.

Main results: The pH-responsive ability of Lipo-HFn enables RepSOX and IPA remain in their desired positions and exert their functions respectively (in brain endothelial cells and brain parenchyma respectively). Thus, it can effectively upregulated tight junction protein expression and enhanced the body's antioxidant capacity simultaneously, breaking the vicious cycle of BBB dysfunction-epileptogenesis and uncontrolled inflammation-epileptogenesis.

Discussion: This designed pH-responsive dissociable nanoparticles successfully achieved microvascular stabilization and inflammatory microenvironment regulation. In vivo experiments validate that Lipo-HFn can prolong latency and reduce the frequency of rats' epileptic seizures.

Conclusion: We believe Lipo-HFn is a promising delivery candidate for the treatment of epilepsy and other brain diseases.



Key Words: epilepsy, blood brain barrier, microvascular stabilization, inflammation regulating

Acknowledgements: The authors gratefully acknowledge the support for this work from the National Key Research and Development Program (Grant No. 2021ZD0201602).

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Conjugation of Cyclic RGD-Modified PEG Chains to Checkpoint Blockade Antibodies Enhances Antitumor Efficacy and Targeted Delivery

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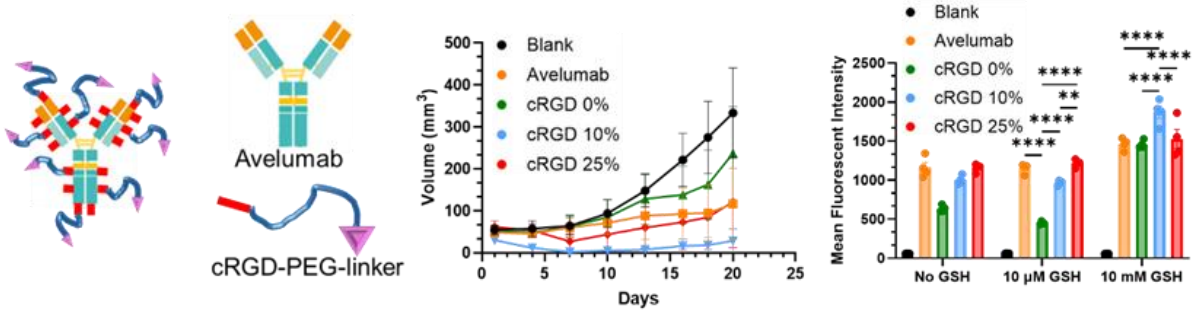
To address limited tumor penetration and off-target effects of anti-PD-L1 antibodies (aPD-L1), we conjugated cyclic RGD (cRGD)-modified polyethylene glycol (PEG) chains to aPD-L1 via a glutathione (GSH)-responsive disulfide bond-containing linker. This design leverages the affinity of cyclic RGD peptides for integrins overexpressed in tumor vasculature and cells, promoting targeted tumor delivery.

In vitro studies demonstrated that antibody-polymer conjugates (APCs) modified with 10% cRGD exhibited significantly enhanced cellular uptake and greater affinity to tumor cell membranes. Biodistribution data indicated that the cRGD 10%-modified APC showed notably higher accumulation in tumors and significantly lower presence in normal tissues compared to unmodified antibodies and APCs with other cRGD ratios. In vivo experiments using KPC tumor-bearing mice further supported these results, demonstrating approximately 30% reduction in tumor volume and an extension of survival by over one week compared to control groups.

These findings highlight the potential of cRGD-modified APCs to markedly improve tumor-specific antibody delivery, enhancing therapeutic outcomes and reducing systemic toxicity.



Key Words: Immune checkpoint blockade (ICB), Anti-PD-L1 antibody, cRGD peptide, Antibody-polymer conjugates (APCs), Tumor-targeted delivery

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The quercetin/paclitaxel loaded nanoparticles as pulmonary drug delivery system for lung cancer

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There are 1.8 million new cases of lung adenocarcinoma and 1.6 million related deaths each year, accounting for approximately 19% of all cancer-related causes of death. Lung cancer has become the leading malignant tumor threatening health and life. About 80-85% of lung cancer patients are non-small cell lung cancer (NSCLC), and over 75% of lung cancer patients are diagnosed in the middle or late stages, with chemotherapy still being the most effective treatment[1]. Paclitaxel (PTX) is widely used in the front-line chemotherapy for cancer, but its therapeutic efficiency is limited by poor water solubility and the following side effects. Previous report revealed that combination therapy has shown good potential in the treatment of lung cancer [2]. And querecetin (QUE) has been reported as a natural bioflavonoid with great antitumor potential. In our study, chitosan nanoparticles (CTS NPs) loaded PTX and QUE were prepared by the ionic cross-linking technique, the two NPs were co-delivered in a certain ratio to reduce the amount of PTX and improve the treatment efficiency. The physicochemical properties of two NPs were studied. TEM showed that QUE NPs and PTX NPs are spherical and uniform distributed and particles-size analysis displayed a particle size of 271.1±9.1 nm and 278.4±7.6 nm, respectively. The drug loading and encapsulation efficiency of QUE NPs and PTX NPs were 11.17±1.12% and 87.73± 4.21%, 13.01±1.41% and 92.04% ± 5.42%, respectively. Moreover, the two NPs displayed similar sustained- profile in PBS (pH 5.5, pH 7.4) and could be successful uptaked into lung cancer A549 cells. All the results above, the combination therapy (QUE/PTX NPs) was more potent than NPs alone and could provide a promising vehicle for the treatment of lung cancer.

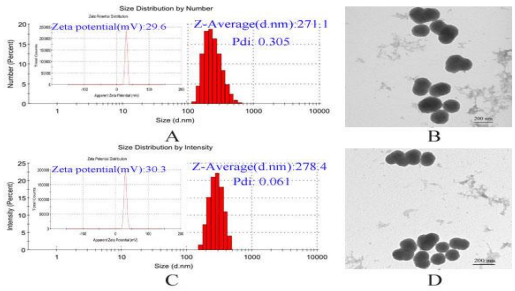

Fig.1: The size distribution, PDI, Zeta potential (A, C) and the morphology using TEM (B, D) of QUE NPs and PTX NPs.

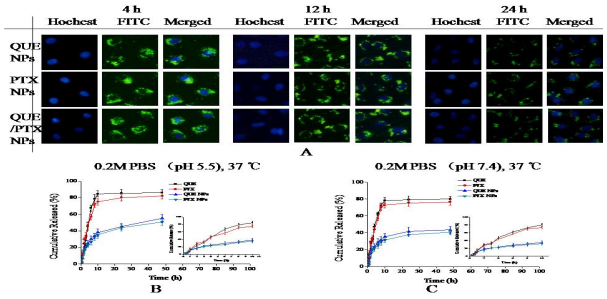

Fig.2: The uptake of cell of QUE NPs and PTX NPs after incubated for 4 h, 12 h, 24 h (A). The in vitro release of free QUE, free PTX, QUE NPs and PTX NPs in pH 5.5 (B) and 7.4 (C) for 48 h

Key Words: Paclitaxel, Querecetin, Chitosan nanoparticles, pulmonary drug delivery system

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Nanoparticle-mediated Drug Delivery System for Anti-cancer Therapy

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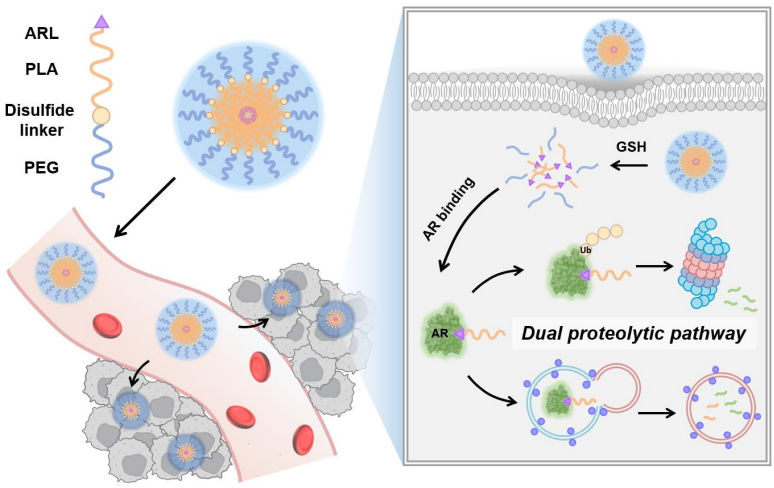
Nanoparticle-mediated drug delivery systems have emerged as highly adaptable platforms capable of integrating multiple therapeutic modalities into a single system. By combining precise targeting, enhanced cellular uptake, and controlled release, these platforms enable advanced strategies in cancer therapy, including targeted protein degradation, photodynamic therapy, and adoptive immune cell modulation.

In this study, we explore innovative nanoplatforms that exemplify this versatility. First, we present a polymeric nanoparticle system in which the polymer itself acts as a degrader, unifying the functions of drug and delivery vehicle to efficiently degrade oncogenic protein. This self-assembling nanoparticle demonstrated effective tumor accumulation and significant tumor suppression in vivo. Furthermore, leveraging the gene delivery capacity of nanoparticles, we developed CAPRN for in situ anti-PD-L1 antibody production with laser-triggered release, and a lipopolyplex-based system (pUnivody@LPP-PBA) to express Fc fragments on tumor cells, thereby activating natural killer (NK) cells in an antigen-independent manner. In vivo experiments confirmed that these smart delivery systems effectively reprogrammed the tumor microenvironment by enhancing T cell infiltration, activating NK cells, and inducing potent anti-tumor immune responses across multiple cancer models.

Overall, these findings highlight the potential of multifunctional nanoparticles as active therapeutic agents capable of gene delivery, protein degradation, and immune modulation, offering a promising platform for next-generation precision cancer nanomedicine.



Key Words: Drug delivery, Nanoparticle, Targeted protein degradation, Gene delivery, Cancer immunotherapy

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Genetically engineered cell membrane-derived vesicles for disease therapy

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Cell membrane-derived vesicles (CMVs), encompassing both naturally occurring extracellular vesicles (EVs) and artificially engineered extracellular vesicles (aEVs), are nanoscale particles secreted by living cells. Owing to their stable lipid bilayer structure, exceptional biocompatibility, and low immunogenicity, these vesicles hold immense promise for applications in drug delivery, regenerative medicine, immunomodulation, and disease diagnostics. Although CMVs inherit certain biological characteristics from their parent cells, their intrinsic functionality often proves inadequate to meet specific therapeutic demands, such as tissue-specific targeting, precise cellular signaling modulation, or efficient delivery of exogenous therapeutic agents. o overcome these limitations, engineered modification strategies—including genetic engineering, chemical conjugation, and hybrid membrane fusion—have been developed to equip CMVs with customized functionalities, thereby broadening their therapeutic potential. Among these approaches, genetically engineered CMVs designed for targeted biotherapeutic delivery have attracted growing interest. Genetically modified CMVs for organ-specific targeting, signal transduction regulation, and the delivery of biomacromolecules and small-molecule drugs. Furthermore, we summarize the therapeutic efficacy of engineered CMVs in treating various diseases, including cancer and metabolic disorders such as diabetes.

Key Words: EVs, genetically engineering, biomedicine, drug delivery

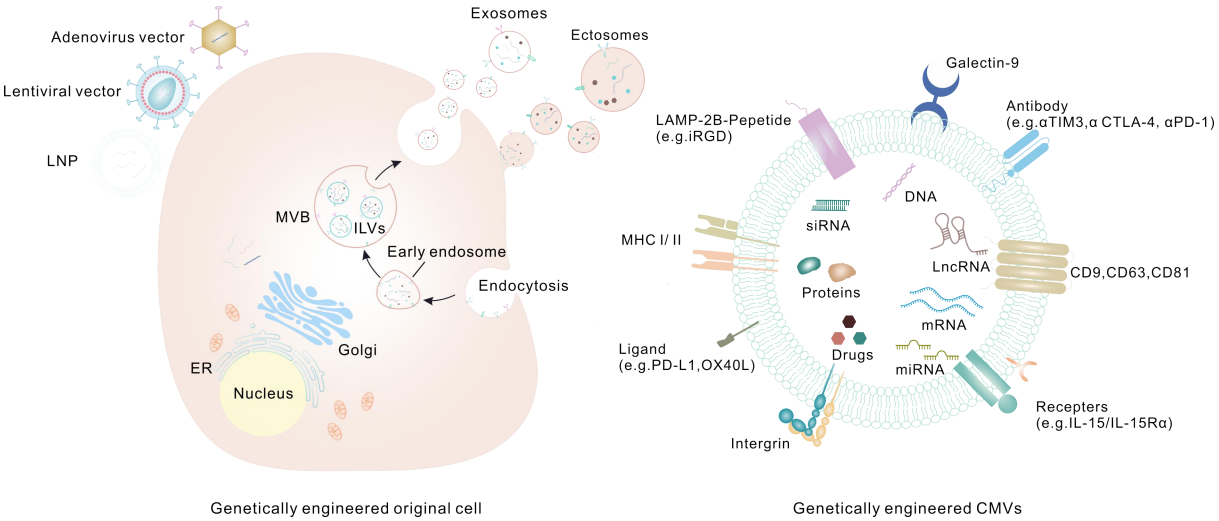

Figure 1.Schematic diagram of genetically engineered modification mechanism of CMVs. (A) Strategies for modifying CMVs by genetic engineering; (B) Transfection and delivery of gene or microRNAs sequence via vectors including LNPs and vectors are core steps in the process of cell genetic engineering. Hereafter, the donor cell's biosynthetic machinery is employed to produce specific biomacromolecules which will execute specific functions inside and outside the cell. Thus, CMVs generated from original cells were modified to load exogenous biotherapeutics and used for disease treatment through genetic engineering methods;

Sandridge-Structured Silk Fibroin Microneedles with High-Capacity Insulin Loading for Enhanced Diabetes Therapy

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Abstract

Diabetes mellitus, a chronic metabolic disorder with escalating global prevalence, continues to rely on insulin replacement therapy as the cornerstone for managing type 1 and advanced type 2 diabetes. However, conventional subcutaneous injections face challenges such as poor patient compliance, risks of local lipohypertrophy, and difficulties in precise glycemic control, while oral administration is hindered by gastrointestinal enzymatic degradation and low bioavailability (<1%). Transdermal microneedle delivery systems have emerged as a promising alternative due to their painless application and ease of use, yet their clinical translation remains limited by low drug loading capacity and significant burst release effects. Inspired by the hierarchical architecture of natural biomaterials, this study innovatively designed a sandwich-structured silk fibroin (SF)-based microneedle (SF-MNs) system to achieve high-efficiency insulin loading and intelligent release via a biomimetic multi-level assembly strategy. The microneedle tips were fabricated using proline-blended SF to form a Silk I crystalline structure, while the base layer incorporated a hyaluronic acid (HA)-insulin reservoir. A final SF coating was applied to construct the sandwich-like architecture. In vitro and in vivo experiments demonstrated excellent skin-penetration capability (mechanical strength: 4.75 ± 0.28 N/needle) and negligible inflammatory response. The SF-MNs exhibited clinically relevant insulin stability over 60 days and sustained drug release profiles. This work provides an innovative strategy for developing high-performance, safe transdermal insulin delivery systems with significant translational potential.

Key Words: Silk fibroin, Microneedle, Sandridge-Structured, Insulin

Symposia 14

Electrospinning Biomaterials

Layer-by-layer assembly of chitosan/lentinan polysaccharide nanofibrous membranes for antimicrobial and tumor synergistic therapy after lung surgery

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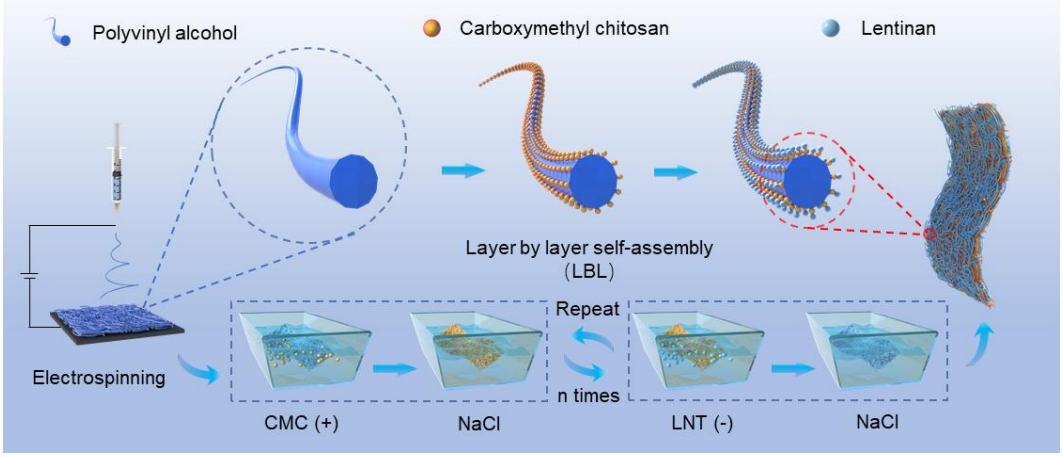
Abstract:

Postoperative lung infection and metastasis of residual cancer cells are the main challenges for postoperative rehabilitation of lung cancer patients. In this study, to address the limitations of traditional antimicrobial materials, such as poor biocompatibility and lack of anticancer function, a bioactive material with dual-functional properties of postoperative antimicrobial and tumor cell inhibition was innovatively constructed by composite modification of the natural polysaccharides chitosan (CS) and shiitake mushroom polysaccharides (LNT) onto nanofiber membranes through layer-by-layer self-assembly (LBL) technology. Characterization of the material showed that the fiber diameter increased and the surface became rough after 10 deposition cycles. The zeta potential on the surface of the nanofiber membrane showed regular oscillations of positive and negative alternation. In addition, the tensile strength of the fiber membrane was found to be as high as 3.5 MPa after mechanical property testing, and the mechanical properties were still good after 3000 cycles of cyclic stretching, confirming the stable hierarchical assembly structure. In vitro experiments showed that the modified nanofiber membrane inhibited Staphylococcus aureus (*S. aureus*) and Escherichia coli (*E. coli*) by 96.65% and 98.89%, respectively, and induced apoptosis in lung cancer cells (A549 and NCI-H1299) with a 24 h inhibition rate of more than 23%. In addition, the material demonstrated good biocompatibility (cell survival >90%) and blood safety. This study provides a new strategy for novel functionalized dressings for integrated postoperative anti-infection and anti-recurrence treatment of lung cancer, highlighting the clinical potential of synergistic modification of natural polysaccharides and nanostructural design.



Keywords: Chitosan, Lentinan, Layer-by-layer assembly, Nanofiber, Postoperative infection, Inhibition of tumor

Acknowledgements: Natural Science Foundation of Hubei Province (2025AFB673).

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Functionally Graded Scaffold with M2 Macrophage-Derived LncRNA-Encoded peptide: Mechanistic and Therapeutic Evaluation for Rotator Cuff Repair

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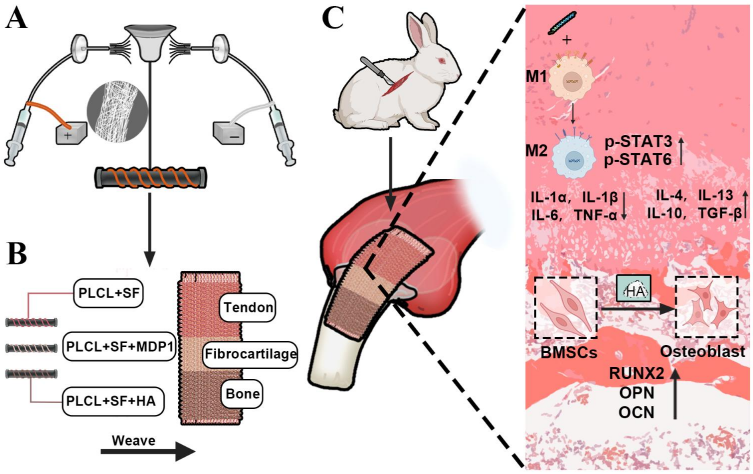
The rotator cuff is prone to tear under degenerative changes or mechanical injury, leading to excessive inflammation, extracellular matrix degradation, and unsatisfactory prognosis. Interleukin-4 (IL-4) was used to induce macrophages polarization toward M2 phenotype. By replacing the activated signaling pathway and performing peptidomic profiling, macrophages-derived peptide 1 (MDP1) has been defined and proven to promote the phosphorylation of STAT3 and STAT6, thereby upregulating the polarization of pro-inflammatory (M1) macrophages to anti-inflammatory (M2) macrophages. A functionally graded scaffold woven from electrospun nanofiber yarns was developed, with MDP1 and hydroxyapatite (HA) loaded onto its corresponding interfaces. During rotator cuff repair process, the scaffold, with mechanical properties (Young's modulus, ca. 280 MPa) comparable to native tendons, prevented rotator cuff re-tearing in an early stage. MDP1 was incorporated into scaffolds to modulate an excessive inflammatory response, while HA was used to enhance bio-mineralization for enhanced osteointegration. Through a multidimensional collaborative repair strategy, this functionally graded scaffold not only mimicked the tendon-bone interface but also promoted tissue regeneration in the damaged region, thereby ultimately enhancing rotator cuff performance. The multifunctionally graded scaffold may offer an invaluable solution to promote tendon-bone healing for rotator cuff tear repair and potentially other related disciplines.



Key words: Electrospinning; Rotator cuff; Tendon-bone interface; LncRNA MM2P; MDP1; Anti-inflammatory; Tissue engineering

Acknowledgments

This research was supported by the Medical-Engineering Interdisciplinary Collaborative Project (Grants No. 2023DHYGJC-YBB04) between Shanghai Tongren Hospital and Donghua University

A novel core–shell with tetradecyl dimethyl benzyl ammonium–modiffed montmorillonite interlayer nanoffbrous membrane and its antimicrobial properties

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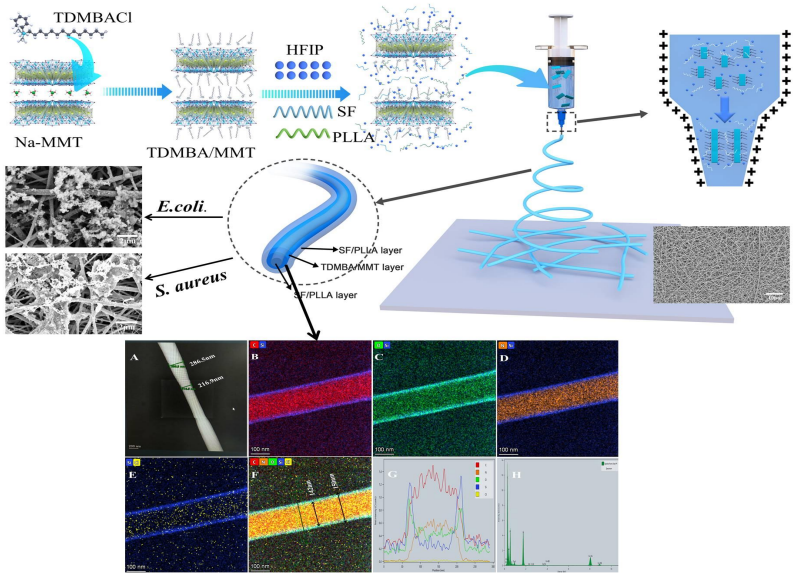
In harsh environments, drug-resistant bacteria can survive by forming biofilms (communities of microbes) on living or nonliving surfaces[1]. Novel antimicrobial nanomaterials have been recognized as promising biofilm inhibitors because their distinguished physicochemical properties restrain the antibiotic resistance mechanism[2] . Oganic montmorillonite (OMMT) is typically fabricated using organic cations via cation exchange reactions to enhance the compatibility of MMT with polymers and expand its interlayer space, enabling the emplacement of interlaminar organic molecules/polymersIn this study, a novel core–shell with a tetradecyl dimethyl benzyl ammonium chloride–modiffed montmorillonite (TDMBA/ MMT) interlayer silk ffbroin (SF)/poly(lactic acid) (PLLA) nanoffbrous membrane was fabricated using a simple conventional electrospinning method. SEM and pore size analyses revealed that this core–shell with TDMBA/MMT interlayer maintained its nanoffbrous morphology and larger pore structure more successfully than SF/PLLA nanoffbrous membranes after treatment with 75% ethanol vapor. TEM and EDS testiffed that the SF/PLLA–TDMBA/MMT nanoffbers exhibited a core–shell with an interlayer structure, with SF/PLLA in the core–shell layer and TDMBA/ MMT in the interlayer. The formation of a core–shell with interlayer nanoffbers was primarily attributed to the uniform dispersion of TDMBA/MMT nanosheets in a solution owing to its exfoliation using hexaffuoroisopropanol and then preparing a stable spinning solution similar to an emulsion. Compared to SF/PLLA nanoffbrous membranes, the core–shell structure with TDMBA/MMT interlayers of SF/PLLA nanoffbrous membranes exhibited enhanced hydrophilicity, thermal stability, mechanical properties as well as improved and long-lasting antimicrobial performance against Escherichia coli and Staphylococcus aureus without cytotoxicity



Keywords: Core–shell with interlayer nanoffber, Montmorillonite, Antimicrobial properties

Acknowledgement

The work was sponsored by the Jiaxing Public Welfare Research Project (2021AY10062)

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The dexamethasone mesoporous polydopamine nanoparticles-based fibrous poly (L-lactide-co-ε-caprolactone)/egg membrane dressings enable skin regeneration

Lu Han[1], Hao Feng[1], Shutao Ma[1], Shuqi Lou[1], Yi Li[1], Jieyin Li[1], Chuhan Zhang[1] , Zhengchao Yuan [a, *], Xiumei Mo [a, *]

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Chronic wound treatment faces challenges like single-functionality and insufficient anti-inflammatory-antioxidant synergy in traditional dressings. This study develops a multifunctional nanofiber dressing (PE@MD) using eggshell membrane (ESM) and dexamethasone-loaded mesoporous polydopamine (MPDA@DEX) to remodel the wound microenvironment and enhance tissue regeneration. PE@MD was fabricated via electrospinning, combining ESM (rich in collagen/antioxidants for ROS scavenging and cell migration) with MPDA@DEX (enabling sustained DEX release for anti-inflammatory/antioxidant effects). The design emphasizes waste resource utilization (ESM) and functional synergy. PE@MD exhibited synergistic anti-inflammatory-antioxidant effects, sustained drug release (64.23% cumulative release over 14 days), low hemolysis (<2%), and enhanced ROS reduction and M2 macrophage polarization. In rat full-thickness wounds, PE@MD achieved 97.99% closure and 64.41% collagen deposition (vs. 70.70% closure and 37.10% collagen in commercial dressings) by day 14. PE@MD synergizes waste-derived ESM and MPDA@DEX to address multifactorial wound healing challenges, offering an efficient, sustainable strategy for chronic wound repair and agricultural by-product valorization.

Key Words: Egg membrane; Mesoporous polydopamine; Electrospinning; Dexamethasone; Wound healing; Tissue regeneration

Acknowledgements: The project was supported by the Songjiang District Committee of Science and Technology, Shanghai, China (Grant No.2023SJKWGG040), Science and Technology Commission of Shanghai Municipality, China (20DZ2254900), Sino German Science Foundation Research Exchange Center, China (M-0263), and China Education Association for International Exchange (2022181). This project was supported by Researchers Supporting Project Number (RSP2024R65), King Saud University, G. Cai et al. Chemical Engineering Journal 500 (2024) 156555 16 Riyadh, Saudi Arabia. This project was also supported by the Taishan Scholars Program of Shandong Province (tsqn201812141), Shandong Provincial Natural Science Foundation (ZR2021MH004).

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Modified Highly Elastic 3D Nanofiber Embolic Scaffolds for Precise In Situ Embolization Therapy

Pengfei Cai[1,2], Lei Cao[1], Yangfan Ding[1], Bernd Rolauffs[2], Melanie Hart[2], Xiumei Mo[1], Shoubao Wang[1], Binbin Sun[1]

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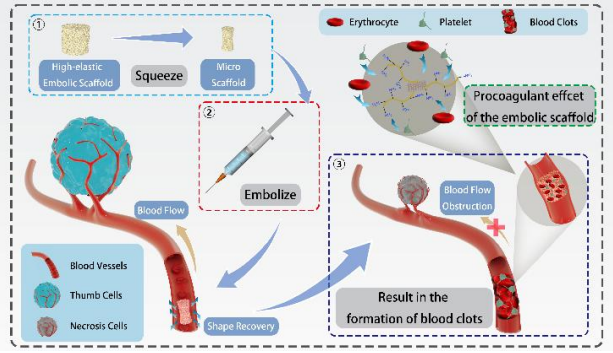
Key words: nanofibers, scaffold, embolic agent, coagulant, transcatheter arterial embolization

Introduction: In the past decades, transcatheter arterial embolization (TAE) has been considered as a practical and effective treatment for aneurysms and arteriovenous malformations due to its relatively less invasive and more purposeful treatment. However, commonly used vascular embolization materials such as gelatin sponge particles may have risks such as particle regurgitation and non-target embolization risks during the application. Based on the above background, we tried to construct a nanofibrous embolization scaffold with high elasticity. The good elasticity allows it to be squeezed to the right size for smooth interventional treatment of blood vessels. After entering the vessel, the embolic scaffold quickly absorbs blood and rebound to its original size and perform its coagulation function to achieve successful embolization of the target area.

Research Design: PCL/Gelatin nanofiber membranes are obtained by electrostatic spinning. Subsequently, the nanofibers are homogenized at high speed and cast into shape and then lyophilized to obtain the uncross-linked 3D scaffolds. The un-lyophilized scaffolds are soaked with glutaraldehyde solution to achieve cross-linking of the scaffolds to obtain the elastic three-dimensional scaffolds. The scaffolds are subsequently modified with lysine and polyethyleneimine to impart procoagulant function to finalize the preparation of highly elastic embolic scaffolds.

Results & Discussion: The embolic scaffold has good physicochemical properties and biocompatibility. The excellent mechanical properties ensure its mechanical stability after entering the vessel, effectively avoiding problems such as regurgitation or off-targeting. The good biocompatibility ensures its safety in the body after implantation. In addition, the embolic scaffold has good platelet and erythrocyte adhesion ability, which allows it to promote coagulation to accelerate thrombus formation and achieve embolization in the target area. The successful embolization of the embolization scaffold is also demonstrated in an in vivo rabbit ear embolization model.

Conclusions: In this study, a highly elastic, pro-coagulant nanofibrous embolic scaffold is designed. Its good biocompatibility and pro-coagulant ability can ensure its thrombus formation after entering the body. More importantly, its proper mechanical properties and excellent shape recovery can effectively overcome the drawbacks of traditional particle embolic agents and avoid the risk of off-target embolization and other risks. It is foreseeable that this embolic scaffold is expected to play an important role in the field of interventional therapy.



Scheme. Schematic diagram of embolic scaffold intervention.

Development of fibre-microsphere composite system for modulation of cell behaviour and tissue regeneration

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Scaffolds integrated with topological cues and biological effectors have attracted widespread attention in neural tissue engineering because of their capability of promoting neurite growth and accelerating cell migration[1]. Among others, the electrospinning technique provides a versatile and effective strategy to fabricate scaffolds suitable for nerve repair, which can achieve expected components, secondary structures, as well as fiber alignments by adjusting the electrospinning parameters or post treatments. Here we report the development of a class of nanofibrous scaffolds that can enhance the outgrowth and extension of neurites as well as neural stem cell migration owing to the guidance from topological cues and biological effectors (Fig. 1). The decoration of secondary structures (*i.e.*, nanoscale protrusions or grooves; electrosprayed microparticles) on electrospun fibers or fiber yarns can be obtained. Then, bioactive proteins and growth factors can be coated on or encapsulated in the fiber materials to construct the functionalized nerve guidance conduits (NGCs). We showed that the uniaxially aligned PCL/SiO_2 nanofibers promoted the neurite outgrowth of SH-SY5Y cells. After coating Gal-1, the neurite length extending from SH-SY5Y cells was further increased. We also observed that the migration of neural stem cells from the neurospheres was significantly accelerated along the direction from central toward the peripheral areas on the radially aligned PCL/SiO_2/Gal-1 nanofibers. Further, we designed and fabricated a class of uniaxially aligned nanofiber yarns welded with electrosprayed microparticles to guide the directional growth of axons and the migration of neural stem cells. The microparticles were further modified by loading nerve growth factors in the core and then deposited on the nanofiber yarns. Owing to the synthetic effects provided by the physical and biological signals, the migration of neural stem cells was significantly accelerated. Taken together, such nanofibers decorated with topographical and biochemical cues would have great potential in nerve repair and related applications involving neurite extension and stem cell migration.

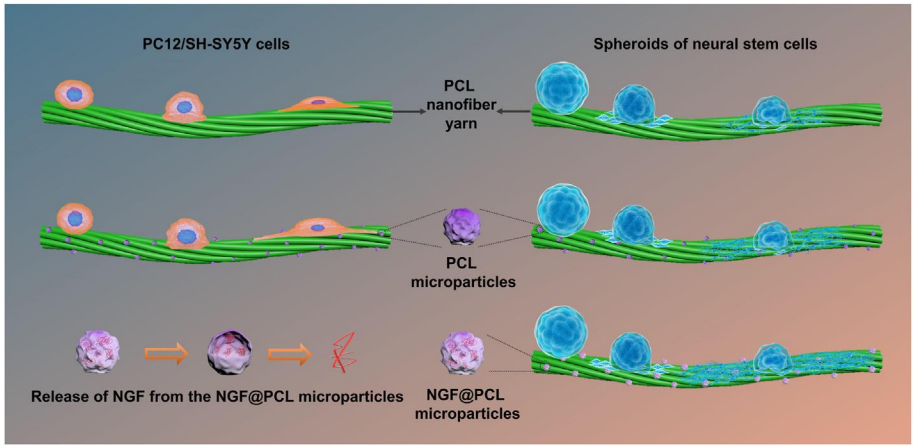

Fig. 1. Schematic illustration showing the axonal growth of neural cells and cell migration from the spheroids of stem cells after cultured on the nanofiber yarns and yarns welded with microparticles.

Key Words: Electrospun fibers, Neurite extension, Cell migration, Nerve repair

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Osteogenic surgical sutures for tendon traction and fixation: A model of achilles tendon sleeve avulsion

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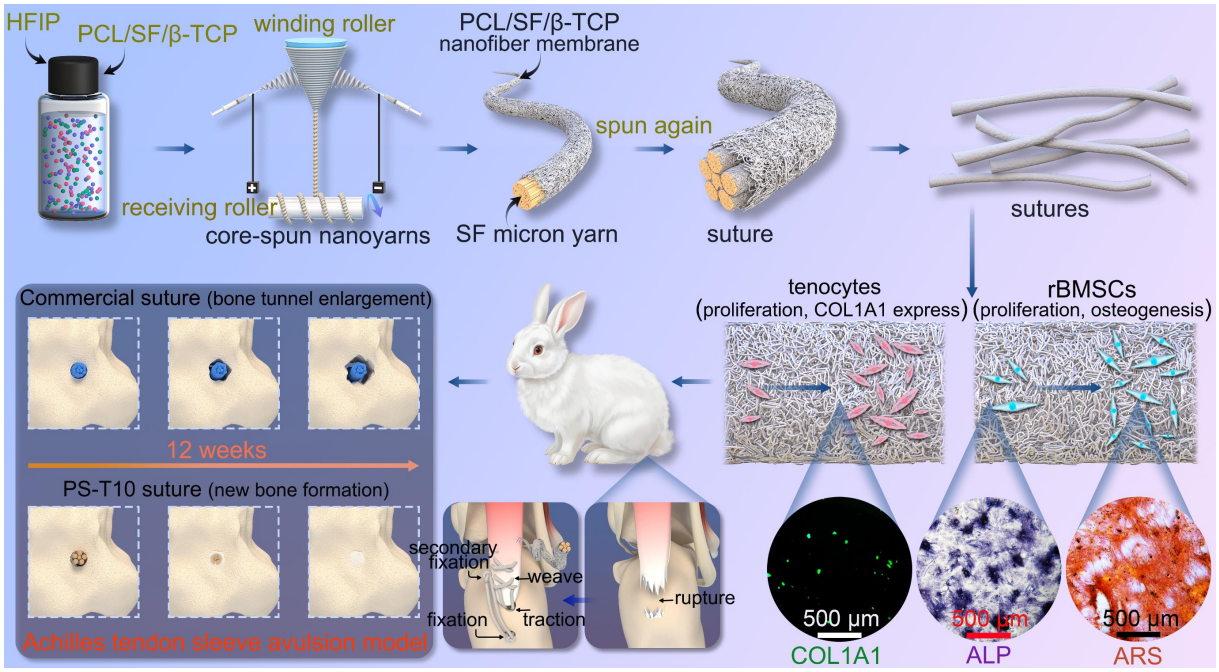
Abstract Currently, the repair of Achilles tendon sleeve avulsion is a challenge due to their limited research and particularly difficult treatment. In tendon repair surgery, the construction of bone tunnels is required for the suspensory fixation of ruptured tendon by sutures. However, due to the biologically inert of commonly used tendon sutures, postoperative fixation instability, bone tunnel enlargement, and even tendon reconstruction failure can easily occur under stressful conditions. In this study, core-spun nanoyarns containing β-tricalcium phosphate (β-TCP) were prepared by electrospinning to serve as surgical sutures for tendon traction and fixation. The suture of 6 core-spun nanoyarns spun again into one strand had stronger mechanical properties, which could effectively pull the tendon. The silk fibroin micron yarn of the suture core layer and the polycaprolactone/silk fibroin/β-TCP nanofibers of the shell layer demonstrated favorable biocompatibility, which facilitated cell adhesion and expression in the tendon and bone. In the repair surgery of the Achilles tendon sleeve avulsion in rabbits, compared with non-degradable and high mechanical properties commercial sutures, the β-TCP in the nanofibers of sutures could induce osteogenesis, thereby reducing the gap in the bone tunnel and preventing enlargement of the bone tunnel. In conclusion, the suture could weave the ruptured tendon, fix the tendon to the bone, promote the formation of new bone in the bone tunnel, avoid the instability of the existing commercial sutures to the bone tunnel, and ultimately improve the success rate of tendon repair surgery.



Key Words: tendon repair, suture, traction, fixation, osteogenesis

Acknowledgements: Science and Technology Commission of Shanghai Municipality, China (20DZ2254900), Sino German Science Foundation Research Exchange Center, China (M-0263), and China Education Association for International Exchange (2022181).

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Electrospun Nanofibrous Biomaterials for Advanced Bio-Interfacial Design in Wound Treatment

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Abstract: Wound treatment continues to pose significant challenges in modern healthcare, it is necessary to develop effective wound healing and hemostatic materials. Electrospun nanofibrous, which mimic the nanofibrous architecture of the natural extracellular matrix, provide an ideal platform for promoting cell and platelet adhesion. To enhance therapeutic outcomes, it is critical to design functional fibrous biomaterials that establish a suitable material-tissue interfacial microenvironment. In this study, we focus on advancing bio-interfaces by integrating improved biological interfacial properties with mechanical performance. Specifically, we developed Janus nanofibrous patches that combine anti-adhesion and pro-healing functionalities, heat-triggered shrinkable fibrous tapes designed to accelerate wound closure, and self-expanding nanofibrous cryogels for effective hemostasis in deep and incompressible wounds. These innovations demonstrate significant potential for clinical applications in wound treatment.

Abstract: Bio-interfacial, Electrospun, Nanofibrous, Wound treatment

Nanofibrous Biomaterials with Improved Bio-interface for Wound Treatment

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Abstract: Wound treatment remains a significant challenge in modern healthcare. It is necessary to develop effective wound healing and hemostatic materials. Electrospun nanofibrous materials, which mimic the nanofibrous architecture of the natural extracellular matrix, provide an ideal platform for promoting cell and platelet adhesion. To enhance therapeutic outcomes, it is critical to design functional fibrous biomaterials with a suitable material-tissue interfacial microenvironment. We focus on advancing bio-interfaces by integrating improved biological interfacial properties with mechanical performance. Specifically, we developed Janus nanofibrous patches that combine anti-adhesion and pro-healing functions, heat-triggered shrinkable fibrous tapes for accelerating wound closure, and self-expanding nanofibrous cryogels for effective hemostasis in deep and incompressible wounds. The functionalized nanofibrous biomaterials demonstrate significant potential for applications in wound treatment.

Abstract: Nanofibrous biomaterial, Bio-interface, Anti-adhesion, Self-expanding capability, Wound treatment

Composite Aerogel Scaffolds Containing Flexible SiO2 Fiber and Tricalcium Phosphate Enable Skin Regeneration

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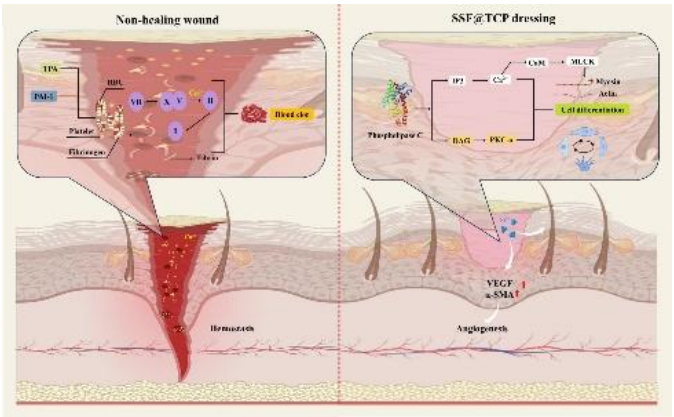
Abstract: Poor hemostatic ability and less vascularization at the injury site could hinder wound healing as well as adversely affect the quality of life (QOL). An ideal wound dressing should exhibit certain characteristics: (*a*) good hemostatic ability, (*b*) rapid wound healing, and (*c*) skin appendage formation. This necessitates the advent of innovative dressings to facilitate skin regeneration. Therapeutic ions, such as silicon ions (Si^{4+}) and calcium ions (Ca^{2+}) have been shown to assist in wound repair. The Si^{4+} released from silica (SiO_2) can upregulate the expression of proteins, such as alpha smooth muscle actin (α-SMA) and vascular endothelial growth factor (VEGF) which are conducive to vascularisation; Ca^{2+} released from tricalcium phosphate (TCP) can promote coagulation alongside upregulating the expression of cell migration and cell differentiation related proteins, thereby facilitating the wound repair. The overarching objective of this study was to exploit short SiO_2 fiber along with the TCP to prepare the TCPx@SSF aerogel and assess their wound healing ability. Short SiO_2 fibers were prepared by electrospinning and blended with varying proportions of TCP to afford TCPx@SSF aerogel scaffolds. The TCP_x@SSF aerogels exhibited good cytocompatibility in a subcutaneous implantation model as well as showed rapid hemostatic effect (hemostatic time, 75s) in a liver trauma model in the rabbit. These aerogel scaffolds also promoted skin repair and exhibited rapid wound closure, epithelial tissue regeneration, and collagen deposition. Taken together, TCP_x@SSF aerogels may be worthy for wound healing.

Keywords: Electrospinning; Aerogel; Wound healing; Hemostatic; Short sclica fiber



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Electrospun Nanofiber for Soft and Hard Tissue Engineering

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The objective of this study is to develop copper-doped flexible silica nanofibers (SiO_2@Cu NF) with multifunctional antibacterial and anti-inflammatory characteristics. The continuous release of copper ions from electrospun membranes is shown to be effective to promote antibacterial and bioactive functions. Nanofibers membranes also exhibit biocompatibility and promote cell growth, angiogenesis, and inflammation modulation. In vivo evaluations further reveal the therapeutic efficacy of SiO_2@Cu NF to promote the structural and functional recovery of the conjunctiva.

We prepared flexible silica-strontium oxide (SiO_2-SrO) nanofibers and poly(lactic acid)/gelatin (PG) fibers using electrospinning and further assembled them into 3D composite aerogel scaffolds (PG/SiO_2-SrO). The scaffolds manifested an ordered porous structure alongside good cytocompatibility, biocompatibility, and biological activity *in vitro*. These scaffolds not only increased the expression of bone-related genes but also enhanced the proliferation and tubule-like network formation of human umbilical vein endothelial cells (HUVECs) *in vitro*. Evaluation in a rat skull defect model demonstrated the potential of composite aerogel scaffolds for bone regeneration and simultaneous osteogenesis and angiogenesis.

The study explores the development of advanced biomaterials for wound healing and bone regeneration. For skin repair, TCPx@SSF aerogels were fabricated by integrating tricalcium phosphate (TCP) with short electrospun silica (SiO_2) nanofibers. These aerogels demonstrated rapid hemostasis (75 s in a rabbit liver model), excellent cytocompatibility, and enhanced wound closure by promoting vascularization and collagen deposition. Concurrently, SSFx@TCP cryogels were engineered for bone regeneration, combining TCP with SiO_2 fibers to form 3D scaffolds with low density, high water absorption, and sustained ion release. These cryogels facilitated cell proliferation, osteogenic differentiation, and angiogenesis-related gene expression. *In vivo*, SSFx@TCP scaffolds significantly enhanced bone formation in rat calvarial defects after 8 weeks. Both systems leverage the synergistic effects of Ca^{2+} (from TCP) and Si^{4+} (from SiO_2) to mimic extracellular matrix functions, offering promising strategies for accelerating wound healing and addressing complex bone defects, thereby advancing regenerative therapies.

Key Words: Electrospinning, Nanofiber, Inorganic nanofiber, Tissue engineering

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Advanced Gas Foamed 3D Nanofiber Scaffolds for Tissue Regeneration

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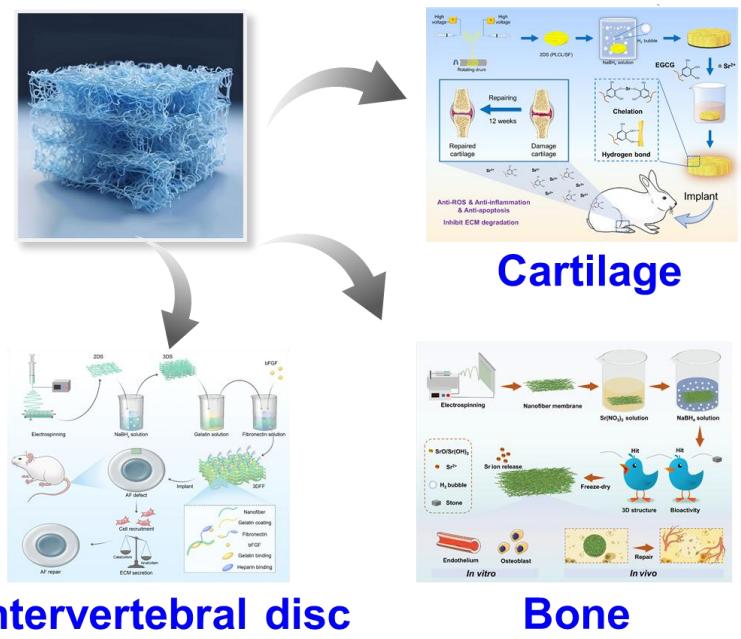
Bone, cartilage, and intervertebral disc defects are common clinical issues, and current treatments have limitations. Electrospun nanofiber membranes mimic the extracellular matrix but have a dense 2D structure that hinders cell infiltration and nutrient diffusion. This study constructs a 3D nanofiber scaffold using gas foaming technology and applies functional modifications to enhance its repair potential. Electrospinning was used to fabricate nanofiber membranes, which were then transformed into 3D porous scaffolds via gas foaming. Functional modifications were introduced to create a better regenerative microenvironment. In vitro characterization included scanning electron microscopy, mechanical testing, and biocompatibility assessment. In vivo validation was conducted using bone, cartilage, and intervertebral disc defect models. Gas foaming successfully created high-porosity 3D nanofiber scaffolds. Compared to 2D membranes, the 3D scaffolds exhibited superior cell adhesion, proliferation, and infiltration capabilities. Strontium-modified scaffolds promoted vascularization and osteogenesis, while metal-polyphenol-modified scaffolds enhanced chondrocyte adhesion, alleviated inflammation, and promoted cartilage matrix secretion [1,2]. Growth factor-modified scaffolds supported intervertebral disc annulus fibrosus regeneration. The functionalized 3D nanofiber scaffold demonstrated good biocompatibility and offers a promising strategy for bone, cartilage, and intervertebral disc repair.



Key Wards: Electrospinning; Gas Foaming; Three-Dimensional Scaffold

Acknowledgements: Laboratory Open Fund of Key Technology and Materials in Minimally Invasive Spine Surgery (2024JZWC-YBA01)

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Symposia 15

Functional Materials for Biomedical Engineering

Surface Engineering Unlocks Drug Loading and Controlled Release

Dongfei Liu[1], Pei Zhang[1], Qingqing Huo[1], Tianhe Huang[1], and Hélder A. Santo[2]

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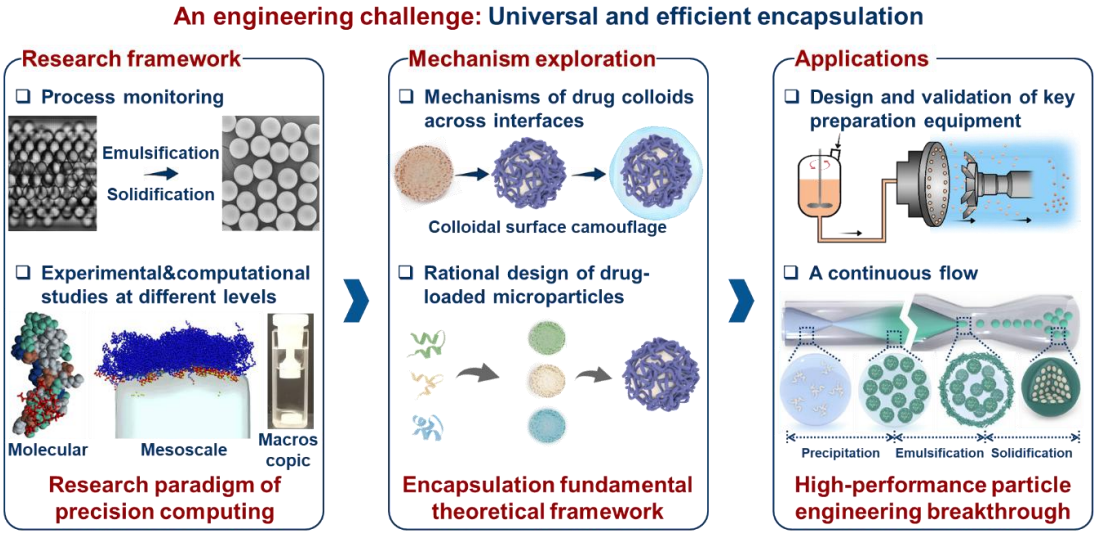
Particulate formulations (e.g., microspheres, nanoparticles, micelles, liposomes) are valuable for controlled drug absorption and distribution. Efficient drug loading and controlled release are critical for regulating drug pharmacokinetics, potentially extending drug half-life, reducing dosing frequency, and improving patient compliance, particularly for metabolic disorders and malignant tumors. However, challenges in achieving efficient drug loading and precise controlled release currently limit their clinical potential. Our research addresses these limitations by investigating drug-carrier interactions across molecular, mesoscopic, and macroscopic scales. This has led to a fundamental theoretical framework focused on regulating interface structure to optimize drug partitioning. We introduce the "colloidal surface camouflage" hypothesis as a universal approach for efficient drug loading, overcoming traditional limitations. Furthermore, novel mesoscale structural units enable precise regulation of multilevel and cross-scale interactions, enhancing control over drug loading and release. By elucidating these mechanisms and employing novel strategies, our research aims to optimize particulate drug delivery systems through rational design, maximizing therapeutic outcomes and minimizing side effects. This interdisciplinary research, integrating pharmaceutical technology, physical chemistry, applied physics, materials science, and chemical engineering, seeks to revolutionize drug delivery by unlocking the full clinical potential of particulate formulations for improved patient care and well-being.



Key Words: encapsulation, phase transfer, drug delivery, controlled release, interfacial self-assembly

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Centrifugal Spinning-Derived Biomimetic Aerogel for Rapid Hemostasis with Minimal Blood Loss

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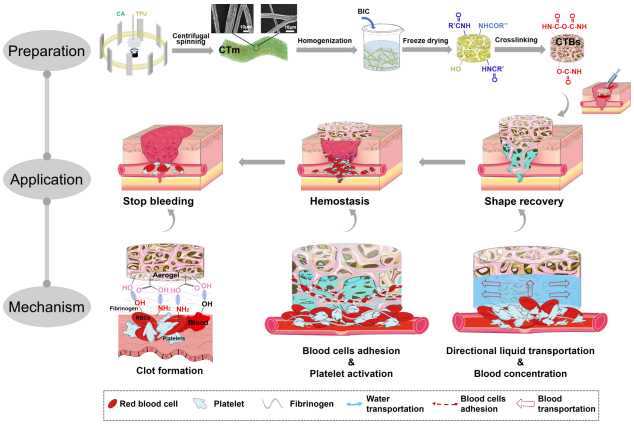
For emergency treatment, especially in situations where rapid and effective hemostasis is required beyond the natural clotting mechanisms, advanced materials designed to reduce bleeding time and minimize blood loss have become an urgent need. Herein, a root hair-inspired aerogel is developed, which is characterized by a 99.99% interconnected pore structure and a three-dimensional network constructed by blocked aqueous isocyanates crosslinked grooved cellulose acetate and wrinkled thermoplastic polyurethane fibers via centrifugal spinning. The aerogel exhibits enhanced water absorption and minimal blood adsorption through rapidly coagulation cascade activation. In vivo studies using rat tail, hepatic and renal injury models demonstrate a substantial reduction in blood loss (~94%) and hemostasis time (~78%) compared to commercial hemostats, offering a potential solution for urgent hemorrhage control, including for patients with coagulopathies.



Key Words: bio-inspired fiber aerogel, centrifugal spinning, structure regulation, hemostasis

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Biomimetic Design of functional activities for bone regeneration

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Natural biomolecules, such as growth factors and antibodies, perform a wide range of functions within biological systems. These functions are critical for resisting external pathogen invasion, modulating the immune environment, and promoting tissue repair, among other physiological and pathological processes. By elucidating the core molecular recognition mechanisms underlying various natural biological activities and employing bionic recognition strategies in the construction of synthetic molecules, it is possible to achieve functionalities analogous to those of natural biomolecules. This approach holds significant implications for uncovering new biochemical mechanisms, enhancing the efficiency of biological molecules, and improving tissue repair and disease treatment. Based on the molecular interactions observed in natural antibody-antigen and receptor-ligand systems, we conducted bionic constructions, mimicking the biometric principles of relevant functional molecules. Through diverse chemical synthesis methods, we achieved artificial design and synthesis of molecules with activities comparable to their natural counterparts, which were subsequently applied to research on bone-related tissue regeneration. The newly developed artificial bioactive molecules not only address the limitations of current natural active molecules, such as stringent storage requirements and limited lifespan, but also promise to expand the repertoire of strategies for designing functional medical drugs and materials, demonstrating substantial application potential in disease treatment and tissue regeneration.

Key Words: antibacterial activity, multivalency, molecular recognition, osteogenesis, osteoclast inhibition

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Self-Assembled Nanostructures of 3ph-imi[$FeCl_4$] as a Strong Ice Recrystallization Inhibitor

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The development of effective ice recrystallization inhibitors (IRIs) is crucial for applications in cryopreservation, food processing, and materials engineering[1-3]. Inspired by the structure-function relationship of antifreeze proteins (AFPs), we designed and synthesized a series of terphenyl-based ionic liquids, 3ph-imi[X] (X = Cl, Br, NO_3, $FeCl_4$) (Fig. 1(a)), to investigate the role of anion specificity and self-assembled structures in IRI activity.

Transmission electron microscopy (TEM) revealed that 3ph-imi[$FeCl_4$] self-assembles into shuttle-like nanostructures with ordered lattice fringes (Fig. 1(b)). Single-crystal analysis revealed that the spacing between hydrophilic $FeCl_4^-$ anions (≈7.07 Å) closely match the ice crystal lattice spacing. This alignment, combined with hydrophilic/hydrophobic surface domains (Fig. 1(c)), mimics the ice-binding face (IBF) of AFPs[2], promoting hexagonal ice-like hydration layers and inhibiting ice growth via the Gibbs-Thomson effect. Low-field NMR and differential scanning calorimetry (DSC) further demonstrated that 3ph-imi[$FeCl_4$] strongly restricts water mobility (T_2 = 132 ms) (Fig. 1(d)) and reduces ice crystallization enthalpy, confirming its superior IRI performance. Among these, 3ph-imi[$FeCl_4$] exhibited the highest IRI activity, reducing the mean largest grain size (MLGS) by 19.7 ± 3.2% at 1.28 mM, outperforming known inhibitors like Safranine O (Fig. 1(e)). In addition, 3ph-imi[$FeCl_4$] promoted ice nucleation and freezing temperature increases by ~10 °C (Fig. 1(f)).

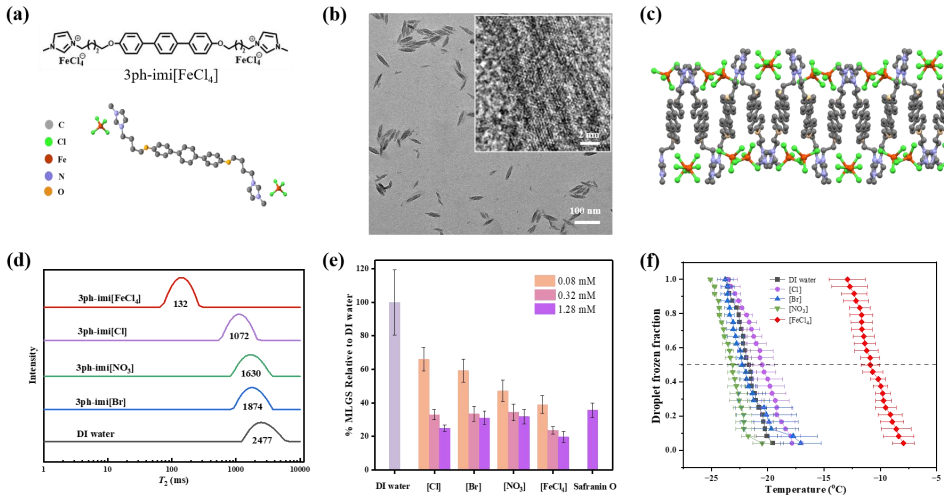

Fig. 1 (a) Molecular structure (b) TEM image and (c) crystal structure of 3ph-imi[$FeCl_4$]. (d) The spin-spin relaxation time (T_2) inversion spectra at 25 °C and IRI activity of 3ph-imi[X] (X= $FeCl_4$, NO_3, Cl, Br). Effect of the (f) 3ph-imi[X] (X= $FeCl_4$, NO_3, Cl, Br) on the frozen fraction during ice nucleation (1.28 mM).

Key Words: ice recrystallization inhibition, ionic liquids, self-assembly, nanostructures

Acknowledgements: National Natural Science Foundation of China (No. 52073201 and 52373152).

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Conductive Fibers and Textiles for Biomedical Applications

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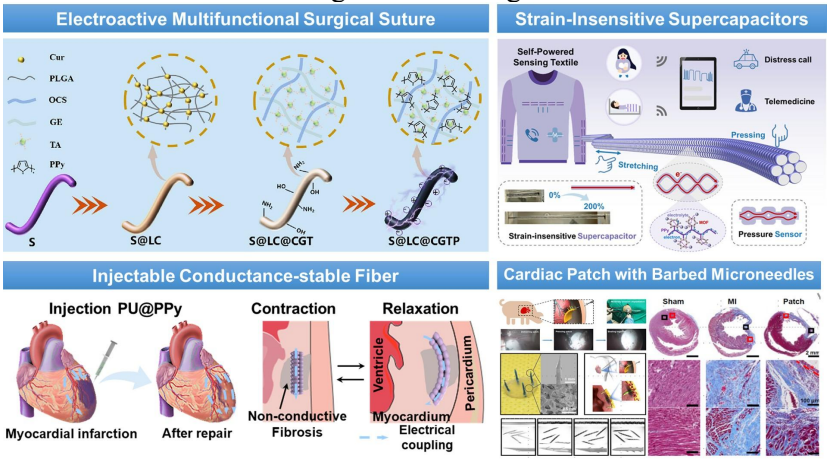
Introduction: The development of conductive biomaterials has been a key focus in biomedical research, aiming to influence cell behavior for tissue regeneration and to enable the monitoring of physiological status through bioelectricity. Conductive fibers have emerged as a promising solution due to their ability to address the mechanical disparities between conductive biomaterials and tissues.

Research Design: A template-assisted interface polymerization method along with a pre-strain technique was proposed to fabricate stretchable polypyrrole (PPy) coatings. A multifunctional suture was designed by incorporating a drug-loaded PPy coating using an *in situ* polymerization method to study its wound healing performance. A sutureless cardiac patch was designed by textile manufacturing process to study its myocardial repair performance.

Main Results and Discussion: This research introduced the theory of sodium sulfosalicylate softening the molecular structure of PPy, and two stretchable conductive coatings, inspired by biomimetic cardiac fiber bundles and maple leaf structures, were designed to enhance the stretchability and insensitive conductivity of the fibers. The application of these fibers in physiological monitoring and stretchable energy storage was verified. Additionally, various drug-loaded PPy conductive coatings were developed, leading to the creation of a series of multifunctional antibacterial and anti-inflammatory conductive medical sutures, which demonstrated the ability to promote wound healing and tissue regeneration. Finally, an oriented injection strategy of conductive fibers and the use of conductive cardiac patches with barbed microneedles to achieve immediate mechanical and electrical integration of infarcted myocardium, thereby restoring post-infarction myocardial electrical communication and enhancing cardiac function.

Conclusion: By innovatively combining conductive materials with therapeutic functions, this research not only expands the biomedical applications of flexible electronics but also provides multifunctional solutions for clinical challenges of tissue regeneration.



Key Words: Conductive Fibers, Wearable Electronics, Tissue Regeneration, Myocardial Repair

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Nanoengineered Red Blood Cells and Stem Cell Derivatives for Targeted Therapy

Jun-Nian Zhou[1], Xue-Tao Pei[1], and Wen Yue[1]

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With the rapid development of interdisciplinary sciences, targeted therapy has expanded beyond the field of oncology treatment. The development of novel targeted therapeutic strategies holds significant research value in crucial life science and health research domains, including tumor therapy, pathogen invasion, and tissue damage repair. Our research group recently developed innovative targeted therapeutic strategies[1-3] in two distinct areas: SARS-CoV-2 invasion of host cells and combined radiation-induced wound damage repair.

(1) Nanoengineered Red Blood Cells Effectively Block SARS-CoV-2 Invasion of Host Cells.

The enzymatic activities enabling binding to Furin, transmembrane serine protease 2 (TMPRSS2), cathepsin L (CTSL), and angiotensin-converting enzyme 2 (ACE2) receptors are essential for coronavirus entry into host cells. Precise inhibition of these critical proteases in $ACE2^{+}$ pulmonary cells during viral infection should prevent activation of viral spike (S) proteins and their subsequent fusion with host cell membranes, thereby blocking viral cellular entry. In this study, we constructed a dual-drug combination (TMPRSS2 inhibitor Camostat and CTSL inhibitor E-64d)-loaded nanocarrier (NC) conjugated with anti-hACE2 antibodies. Utilizing red blood cell (RBC) hitchhiking technology, we developed a novel delivery system termed "Nanoengineered Red Blood Cells" for targeted pulmonary cell delivery. We demonstrated significant therapeutic efficacy of this dual-drug-loaded nanoengineered RBC system in pseudovirus-infected K18-hACE2 transgenic mice. Notably, our modular nanoengineered RBC platform (anti-receptor antibody $^{+}$ NCs $^{+}$ RBCs) can prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entry regardless of viral mutations by precisely targeting key proteases in pulmonary host cells. These findings are expected to facilitate the development of a new series of safe antiviral therapies based on host cell protection.

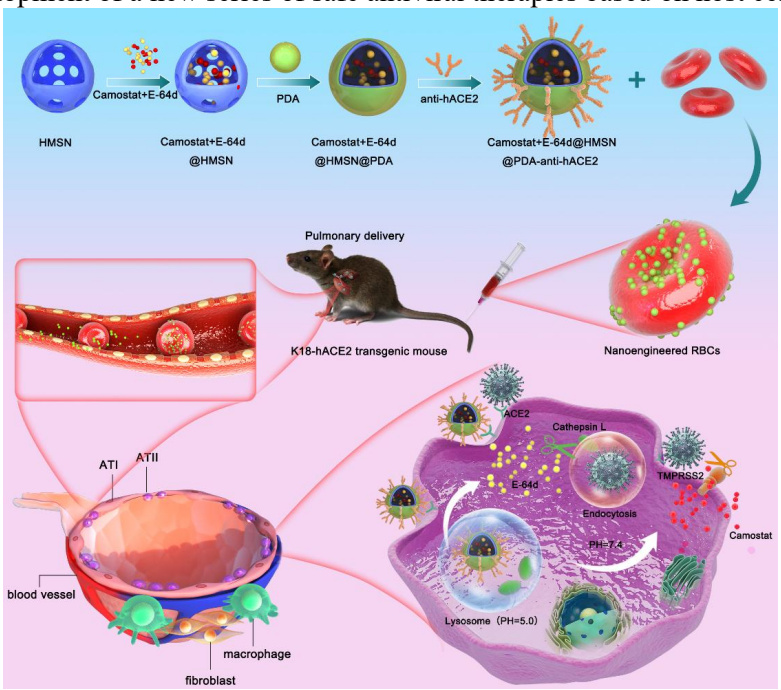

Figure 1. Schematic of nanoengineered RBCs potently blocking SARS-CoV-2 cell entry[2].

(2) Hydrogel Microneedle Patch Loaded with Stem Cell Mitochondria-Enriched Microvesicles Promotes Chronic Wound Healing.

Radiation-induced mitochondrial dysfunction plays a pivotal role in persistent oxidative stress underlying chronic wounds. Growing evidence suggests mesenchymal stem cells' therapeutic effects may primarily derive from their paracrine extracellular vesicles (EVs), positioning EVs as attractive cell-free and safer therapeutic agents. Here, we hypothesized that metformin-treated human adipose-derived stem cells (ADSCs) would enhance mitochondrial biogenesis, thereby increasing secretion of mitochondria-containing EVs ("Met-EVs"). To comprehensively validate Met-EVs' therapeutic efficacy, we established both in vitro and in vivo X-ray-induced mitochondrial dysfunction models. The engineered Met-EVs demonstrated capacity to ameliorate radiation-compromised mitochondrial function through active mitochondrial transfer, including dose-dependent restoration of mitochondrial membrane potential (ΔΨm), elevated adenosine triphosphate (ATP) levels, and reduced reactive oxygen species (ROS) generation. Furthermore, we developed a Met-EVs-loaded decellularized adipose matrix (DAM) combined with hyaluronic acid methacryloyl (HAMA) hydrogel microneedle patch (MNP), which enables controlled loading and sustained release of Met-EVs with their mitochondrial cargo into irradiated wound tissue, effectively mitigating mitochondrial dysfunction. In vivo studies revealed Met-EVs' ability to promote macrophage polarization toward the anti-inflammatory and regenerative M2 subtype, accelerating healing of radiation-damaged skin in murine models. Collectively, the therapeutic efficacy of Met-EVs@DAM/HAMA-MNP demonstrated in this study shows significant clinical potential for chronic wound management.

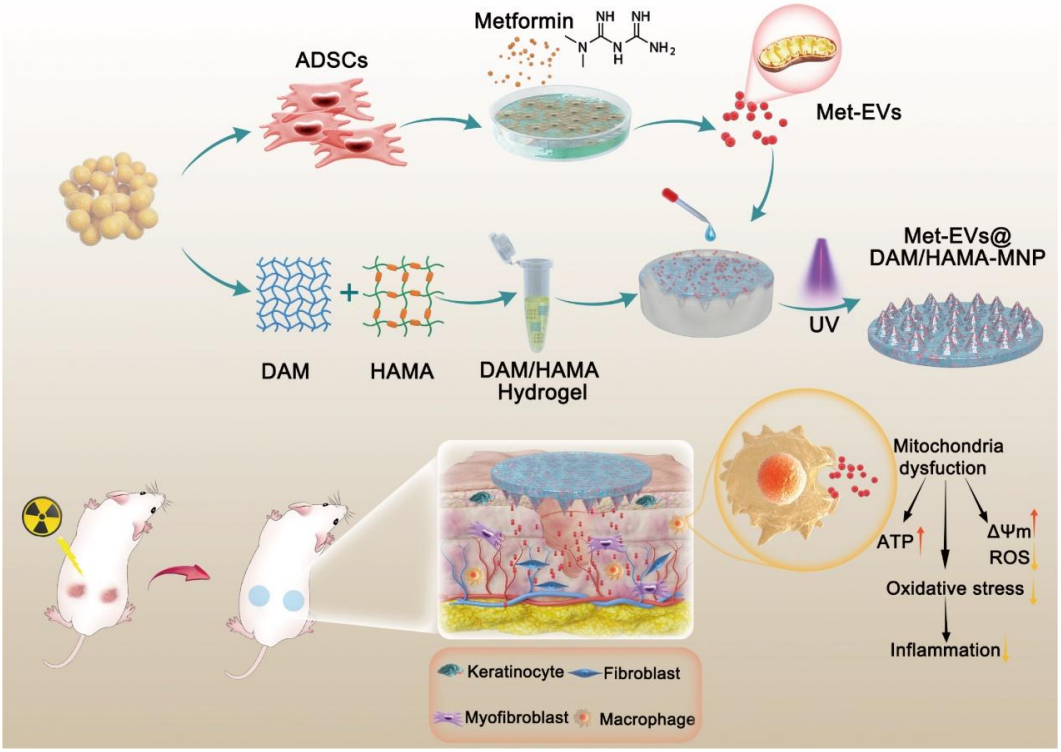

Figure 2. Schematic illustration of the fabrication of Met-EVs@DAM/HAMA-MNP and skin wound treatment in a mice model[3]. Met-EVs@DAM/HAMA-MNPs can continuously and effectively deliver EVs containing active mitochondria to irradiated wound tissues to improve mitochondrial dysfunction by increasing ATP production, decreasing ROS content and oxidative stress pressure, and promoting macrophage polarization from the pro-inflammatory M1-subtype toward the M2-subtype with anti-inflammatory and wound healing functions in skin wound tissues

Key Words: Nanoengineered Red Blood Cells, Mesenchymal Stem Cells, Extracellular Vesicles, Mitochondria, Targeted Therapy

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Efficient Encapsulation and Controlled Release of Drugs in Micro- and Nanoparticles

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High drug-loading in polymeric microspheres is critical for their biomedical applications due to reduced excipients administration, minimized side effects, and enhanced therapeutical efficacy. Although thermodynamic factors like drug-carrier material compatibility are well-known to influence the drug loading capacity of polymeric microspheres, they are not able to explain the huge difference in drug loading degree observed for polymers and drugs with similar interactions.

In this study, based on the droplet microfluidic platform, we investigated the single droplet solidification process. The results indicated that amorphous polymers can hinder drug diffusion during droplet solidification compared to crystal polymers, resulting in a higher drug loading degree. Next, we applied this principle to improve the drug loading capability of crystal polymers (PCL and PLLA) by random co-polymerization (PCL-PLLA), achieving up to 22.2 times increased drug loading degree. Moreover, PCL-PLLA microspheres with high content of indomethacin exhibited superior therapeutical efficacy in the treatment of gout arthritis.

Overall, our results offer insights into the impact of polymer crystallization on droplet solidification kinetics, which consequently affects the drug loading capacity. These findings provide guidelines for the development of polymers for efficient drug encapsulation.

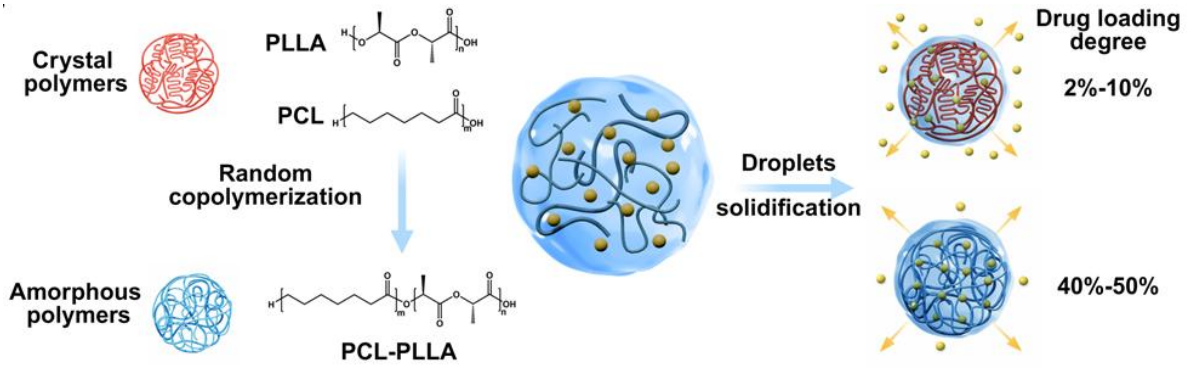

Fig. 1 Influence of the crystallization property on the droplet solidification and drug loading degree.

Key Words: high drug loading, controlled release, microparticle, nanoparticle, microfluidics

Acknowledgements: Prof. Hélder A. Santos, Xiangliang Yang and Dongfei Liu are acknowledged.

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Tuneable Methacrylated Recombinant Human Collagen Hydrogels for 3D Stem Cells Culture and application in wound healing

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Objective: Recombinant human collagen holds broad application prospects. We developed a multifunctional recombinant human collagen using synthetic biology and constructed stiffness-tunable recombinant human collagen-based hydrogels to investigate their mechanical effects on adipose-derived stem cell (ADSC) behavior and their therapeutic potential in full-thickness wound repair.

Methods: Recombinant human type XVII collagen (rhCol) was synthesized and characterized for biosafety and its ability to promote ADSC proliferation, adhesion, migration, and secretion. Methacrylated recombinant human collagen (rhCol-MA) hydrogels were fabricated via chemical modification. By adjusting rhCol-MA concentrations, two hydrogels with distinct stiffness levels (soft: 0.1 kPa, hard: 3 kPa) were generated. The effects of soft/hard hydrogels on ADSC behavior during 3D culture were explored. ADSC-laden hydrogels were further applied to acute full-thickness wounds in nude mice to evaluate their reparative efficacy.

Results: Successful synthesis of recombinant human type XVII collagen was confirmed by time-of-flight mass spectrometry (TOF-MS) and Fourier-transform infrared spectroscopy (FTIR). The recombinant collagen demonstrated excellent biocompatibility and enhanced ADSC proliferation, adhesion, migration, and secretory activity. Soft hydrogels (0.1 kPa) promoted ADSC proliferation, while hard hydrogels (3 kPa) induced chondrogenic differentiation. Compared to 2D culture, 3D hydrogel cultures preserved ADSC stemness while significantly enhancing migration. In vivo experiments revealed that both hydrogel-only and hydrogel+ADSC groups accelerated wound healing in nude mice, with the hydrogel+ADSC group showing superior efficacy.

Conclusion: Recombinant human type XVII collagen, as a novel human-derived collagen, exhibits multifunctional biological properties (promoting stem cell proliferation, secretion, adhesion, and migration). The modified recombinant collagen-based hydrogels possess excellent biocompatibility and tunable mechanical properties, enabling long-term stem cell survival. These hydrogels serve as effective stem cell carriers for wound repair applications.

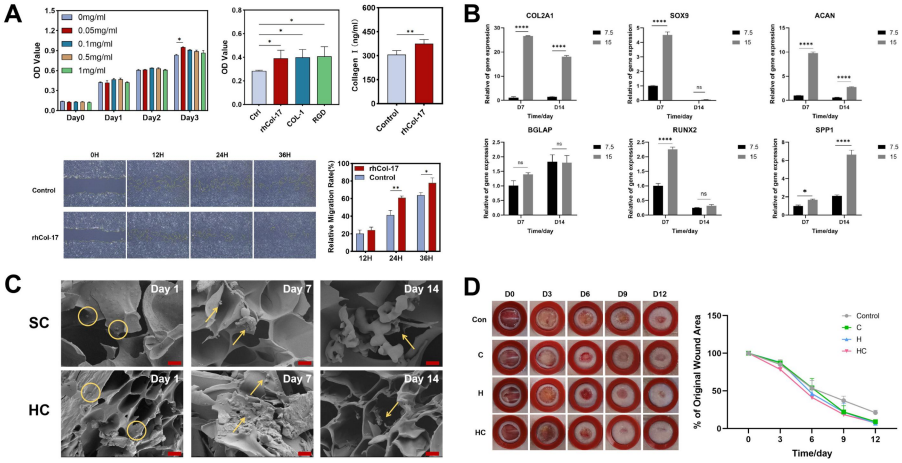

Fig.The biological effects of recombinant human collagen(A) and the spreading (B) and differentiation (C) of stem cells in hydrogels with different hardness of recombinant human collagen hydrogel and (D)the application of hydrogels loaded with cells in wound repair.

Key Words: Hydrogel; Adipose-derived stem cells; Wound repair; Recombinant human collagen

Acknowledgements: This work was supported by the Shanghai Municipal Health Commission （20244Z0009）

Photocrosslinkable polymers for tissue regeneration

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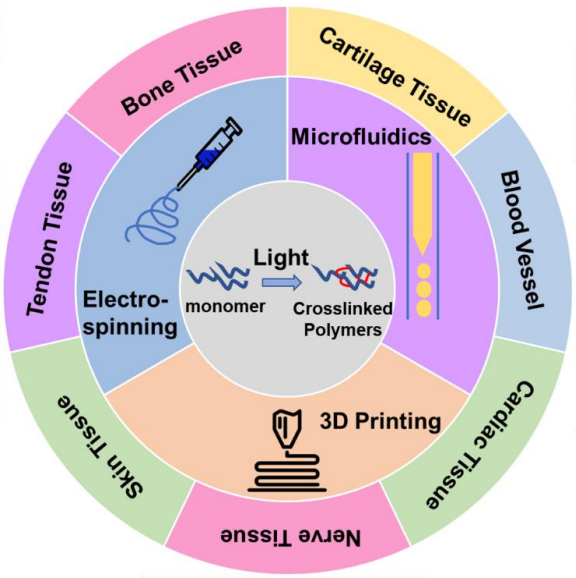
Photocrosslinkable polymers are polymers that can be solidified from liquid upon light exposure. They have been employed to fabricate tissue engineered constructs due to the mild conditions for crosslinking, highly tunable mechanical and structural modifiability, printability, biodegradability and biocompatibility. These biomaterials can maintain their structural integrity after biofabrication and provide topological, biochemical, and physical cues to guide cellular behaviors by creating a biomimetic microenvironment.

The emphasis of this talk is placed on how photocrosslinkable polymers can be used to achieve regeneration of diseased or damaged tissues, for example, their fabrication into various scaffolds (electrospun fibers, microspheres, and 3D printed scaffolds) to reconstruct hard tissues like bone as well as soft tissues such as skin. Specifically, assisted by microfluidics, we have developed photocrosslinkable methacrylated gelatin (GelMA) based microspheres encapsulating human mesenchymal stem cells (MSCs) for bone repair. Due to the mild crosslinking conditions, we found that the GelMA microspheres can provide a favourable micro-environment for MSC survival, spreading, migration, proliferation and osteogenesis. In another study, we prepared a periosteum mimicking bone aid (PMBA) by electrospinning photocrosslinkable GelMA with L-arginine-based unsaturated poly(ester amide) (Arg-UPEA), and methacrylated hydroxyapatite nanoparticles (nHAMA). Upon light exposure, the resultant hydrogel fibrous scaffolds can solidify within seconds. Via controlling the crosslinking density, we can control the scaffolds' mechanical and degradation property. The optimal scaffold was found to provide long term structural and functional support and mediation of physiological activity. With the aid of 3D printing, we developed 3D bone scaffolds made of photocrosslinkable nanocomposite ink consisting of tri-block poly (lactide-co-propylene glycol-co-lactide) dimethacrylate (PmLnDMA, m and n respectively represent the unit length of propylene glycol and lactide) and nHAMA. It is discovered that nHAMA can rapidly interact with PmLnDMA upon light exposure within 140 seconds and form an inorganic-organic co-crosslinked nanocomposite network. This bone ink was found to provide good mechanical strength and bioactivity for bone regeneration.

Graphical Abstract



Key Words

photocrosslinkable polymer, electrospinning, microfluidics, 3D printing, tissue regeneration

Acknowledgements
The Hong Kong Research Grants Council (RGC), Health and Medical Research Fund (HMRF), Innovation and Technology Fund of Hong Kong (ITF), National Science Foundation of China (NSFC), Guangdong Basic and Applied Basic Research Foundation, Greata Group Co. Ltd..

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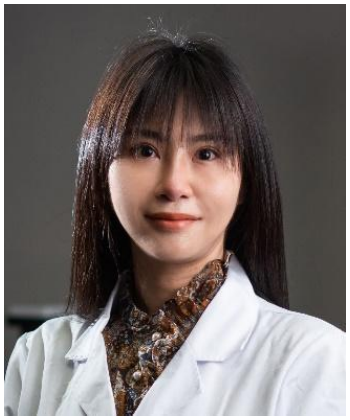
Photo



Biography (91 words)

Professor Xin ZHAO is a distinguished academic in the Department of Applied Biology and Chemical Technology at Hong Kong Polytechnic University. Specialising in translational regenerative medicine, she has authored over 100 articles in leading journals. Recognised globally for her contributions, Professor ZHAO has received numerous accolades, including the National Excellent Young Scientist 2021, Clarivate Analytics Highly Cited Researchers 2022, and listings in "The World's Top 2% Scientists" by Stanford University for 2023 and 2024. Her impactful research has garnered extensive citations, reflected in her h-index of 62 according to Google Scholar.

Amyloid-Like Assembly Confinement Enhancing Enzyme-Mimicking Catalytic Antibacterial Therapy

Yonghai Feng

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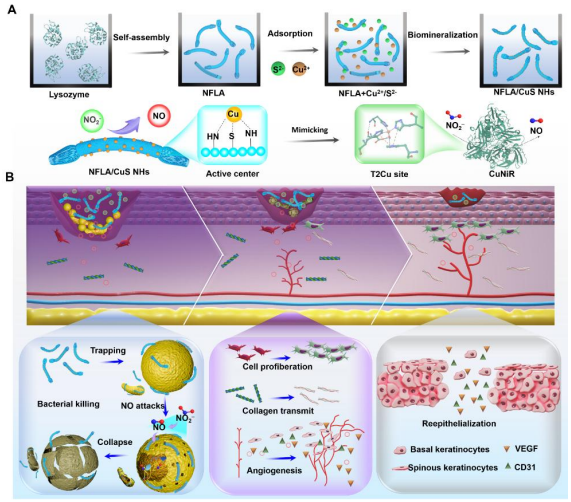
Introduction Nanozymes can effectively circumvent bacterial resistance mechanisms and demonstrate great potential in overcoming antibiotic resistance [1]. Amyloid peptide self-assembly offers multiple advantages in constructing bio-inorganic composite materials, including tunable structures, spatial confinement, strong metal-coordinating residues, cofactor-like catalytic enhancement, and robust bacterial adhesion [2-3]. Therefore, novel artificial enzymes based on amyloid peptide self-assembly may enhance the catalytic antibacterial performance of nanozymes.

Research Design Lysozyme nanofibers (LNF) were synthesized using a deep eutectic solvent method. These nanofibers served as templates for the incorporation of gold and copper ions, followed by the addition of a reducing agent ($NaBH_4$) or a precipitating agent (Na_2S).

Results and Discussion We utilized the spatial confinement and strong metal-coordinating residues of amyloid-like peptide self-assembly to induce the ordered growth and distribution of Au, Au-Cu, and CuS nanoparticles. The self-assembled nanofiber structure enhanced bacterial surface adhesion, while the nanozymes' biomimetic catalytic activity and near-infrared (NIR) photothermal effects synergistically generated highly destructive antibacterial factors (ROS, NO), significantly improving bactericidal efficiency.

Conclusion The one-dimensional LNF/AuCu (or LNF/CuS) composite nanostructures exhibit ultra-strong bacterial interaction, excellent natural enzyme-mimicking activities, and efficient NIR photothermal conversion. Under multiple synergistic effects, they significantly enhance antibacterial performance and accelerate the recovery of infected tissues.



Schematic illustration of LNF/CuS preparation (A) and antibacterial therapy (B).

Key Words: Amyloid peptide; self-assembly; confinement effect; biomimetic catalytic antibacterial

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Targeting lesional macrophages with β-glucan based biomaterials for cardiac therapy

Zehua Liu[1, 2], Han Gao[1, 2], Sen Li[3], Shiqi Wang[2], Wenhua Lian[4], Zhengyi Lan[5], Dan Peer[6], Xianming Deng[4], Ming Ma[5], and Hélder Santos[1, 2]

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Introduction: Cardiovascular diseases are the leading cause of death worldwide, yet conventional drug treatments suffer from poor cardiac retention, requiring further improvement.

Research design: Building on the clinical observation that myocardial ischemia-reperfusion (IR) induces aberrant Dectin-1 expression on macrophages, we designed a series of cardiac-targeted delivery systems using β-glucan, the inherent targeting ligand of Dectin-1. Computational methods were employed to elucidate potential mechanisms for formulation design and optimization.

Main results: We developed two β-glucan-based polymers tailored for delivering small-molecule drugs[1] and gene therapeutics[2]. Using a high-throughput microfluidics workstation integrated with a nanoparticle (NP) characterization system, we screened over 200 formulations, optimizing size, drug encapsulation efficiency, biocompatibility, and macrophage uptake.

To refine formulation design, we created a computational toolbox with an explainable statistical model, offering insights into NP formation, encapsulation efficiency, biocompatibility, and intracellular delivery[3]. This approach enhances property optimization and structure-property relationship interpretation.

Conclusion: These findings highlight the potential of β-glucan-based nanoparticle systems as a precise and effective strategy for macrophage-targeted cardiac therapy

Key Words: Cardiovascular diseases, β-glucan, macrophages, microfluidics, machine-learning

Acknowledgements: Zehua Liu acknowledge the financial support from Academy of Finland, Finnish Red Cross Research Foundation and Finnish Cardiovascular Research Foundation

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Symposia 16

Hydrogels

Continuous Preparation of Robust Hydrogel Fibers

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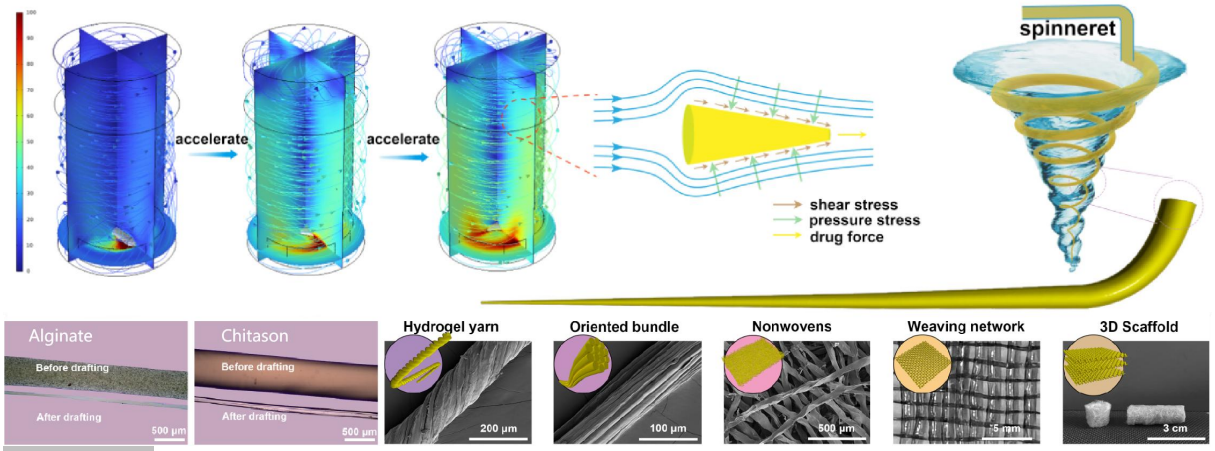
Currently, there is no established spinning technology system that simultaneously addresses the challenges of thick hydrogel fiber diameter, insufficient mechanical properties, and limited production efficiency [1]. Comprehensive research indicates that precise spatiotemporal regulation of crosslinking dynamics in hydrogel networks and molecular chain orientation during spinning, combined with effective axial stretching, constitutes the critical pathway for achieving both thin-denier and high-strength hydrogel fibers [2]. We propose a novel hydrodynamic stretching strategy compatible with wet-spinning and microfluidic spinning platforms, offering flexible and efficient stretching for hydrogel fiber production [3]. This hydrodynamic dynamic stretching strategy successfully overcomes technical bottlenecks in traditional hydrogel fiber fabrication, demonstrating significant advantages in micro/nano-scale regulation and performance enhancement. Through establishing a multi-field coupled stretching model, this approach applies intense shear-stretching effects on fiber fluids, manifested in three key breakthroughs: (1) Broad-spectrum diameter regulation: By optimizing spinneret structural parameters and vortex stretching velocity, the diameter of alginate-based hydrogel fibers was reduced from 500 μm to 35 μm. (2) Molecular network directional reconstruction: The gradient shear field generated during stretching effectively induces axial alignment of polymer chains, increasing fiber birefringence from 0.005 to 0.240. The corresponding breaking strength reaches 12.8 MPa, representing a 15-fold improvement over non-stretched samples and matching the mechanical performance level of natural tendons. (3) Universal high-efficiency fabrication: Achieves a single-nozzle spinning rate of 2110 m/h, with demonstrated process compatibility across five hydrogel systems (including chitosan and polyvinyl alcohol) and synthetic polymer materials.



Key Words: Hydrogel Fibers, Wound Dressings, High-strength, Tissue engineering, Soft drafting

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Hydrogel-based mechano-modulation of the immune system

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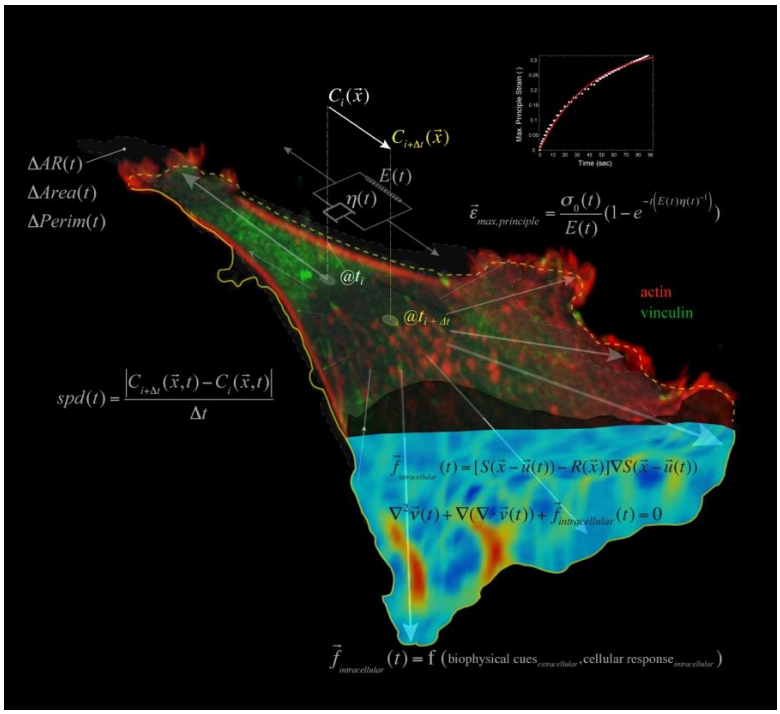
Immune cells are mechanosensitive and a baseline level of physical force, derived and integrated from the various biomechanical cues within the complex immune microenvironment, is required for homeostasis. Biomechanical forces in the form of cell-to-cell, cell-to-matrix and cell-to-shear flow, when perturbed could enhance a positive immune outcome or cause an awry immune response. Biomaterials can be applied to mechanically modulate the immune system. Here we present the mechanoimmunology work performed at the Laboratory for Bioengineering Research and Applications (LIBRA) at New York University Abu Dhabi (NYUAD). As examples, we demonstrate the use of hydrogel-based biomaterials as matrix to investigate basic 3D mechanobiology of immune cells in 3D, transitioning to the reconstruction of biomimetic in vitro models for oncoimmunology and other tissue engineering studies with an immune competency. Furthermore, we employ 2D hydrogels are used to produce cancer-killing lymphocytes that possesses less exhaustion markers, potentially better anti-cancer potency in vivo. We also investigate the 'absence' of such forces and experimentally query the effects of microgravity on immune cells, dabbling with space biology.



Key Words: Hydrogels, Mechanobiology, Immunology, Cancer, Space Biology

Acknowledgements: New York University Abu Dhabi (NYUAD) Faculty Research Fund (AD266)

Cell-adaptable dynamic hydrogels for tissue engineering

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Background and purpose: Although biopolymer-based chemical hydrogels, with biopolymers covalently crosslinked, have been widely used as scaffolds for tissue engineering due to good stability, their permanent network structures and brittleness limit their applications in repairing load-bearing tissues, such as cartilage. In contrast, biopolymer-based supramolecular hydrogels, which are usually formed via self-assembly of physically interacting biopolymers, are usually weak as shown in "inverted vials" instead of freestanding 3D constructs and less stable than chemical hydrogels.
Methods: Herein, we describe a novel host-guest macromer approach based on preassembled host-guest complexations for preparation of biopolymer-based freestanding supramolecular hydrogels.
Results and conclusions: Such hydrogels are solely crosslinked by in situ formed multivalent host-guest nano-clusters, and show significantly reinforced mechanical properties yet still retain desirable supramolecular features. They can self-heal and be re-molded into freestanding 3D constructs which afford effective protection on the encapsulated stem cells during the compression re-molding, making them promising carriers for therapeutic cells that can quickly adapt to and integrate with surrounding tissues of the targeted defects. We demonstrate that such hydrogels supported in situ tissue regeneration via the delivery of therapeutic cells and drugs. Such dynamic hydrogels are not only desirable for potential clinical applications but also useful for 3D culture of cells and organoids to assist basic studies.

Keywords: hydrogel, mechanosensing, tissue engineering

Gene Therapy for Inflammatory Cascade in Intrauterine Injury with Engineered Extracellular Vesicles Hybrid Snail Mucus-enhanced Adhesive Hydrogels

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Background: Early hyper-inflammation caused by intrauterine injury triggered subsequent intrauterine adhesion (IUA). Macrophages are considered to be major regulators of the inflammatory microenvironment. Signal transducers and activators of transcription 1 (STAT1) is a key transcription factor regulating M1 polarization. However, whether STAT1 is involved in the development of IUA by mediating macrophage M1 polarization has not been clarified. However, clinically used hyaluronic acid (HA) hydrogels are prone to slip out of injury sites due to poor bio-adhesion properties. Herein, an engineered extracellular vesicles (EVs) hybrid snail mucus (SM)-enhanced adhesive hydrogels to improve bio-adhesion property is fabricated and M1 macrophage intervention through targeting delivery and STATI silencing is achieved to offer new insights into the prevention and treatment of IUA.

Methods: Multi-omics analysis and immunofluorescence were employed to identify the key target of macrophage-mediated inflammatory responses in IUA and detect the localization of STAT1 in macrophage subtypes. Subsequently, M1 macrophage-targeting engineered extracellular vesicles (FA-EVs) were constructed through FA modification, and STAT1-siRNA was loaded into the EVs via electroporation to form siRNA@FA-EVs. GelMA was blended with different proportions of SM to form a hydrogel, and its morphology was examined using scanning electron microscopy and Fourier-transform infrared spectroscopy. Adhesion and rheological properties were assessed through lap-shear and peeling tests to identify the hydrogel with optimal adhesion. The siRNA@FA-EVs were then loaded into the GelMA/SM hydrogel (GS) to form siRNA@FA-EVs/GS hydrogel, and its biocompatibility and sustained-release behavior were evaluated. In vitro, LPS was used to simulate the inflammatory microenvironment of intrauterine injury. Immunofluorescence staining and flow cytometry were used to assess the proportion of M1-polarized macrophages and the expression of phosphorylated STAT1 (pSTAT1). The supernatant of treated macrophages was used to culture endometrial stromal cells, and the proportion of α-SMA-positive cells was evaluated to assess the differentiation of endometrial stromal cells into myofibroblasts, as well as the secretion of type III collagen and fibronectin 1. The IUA rat model was established, and the therapeutic effects of siRNA@FA-EVs/GS hydrogel on IUA, as well as its impact on endometrial repair and fertility restoration, were evaluated through histological analysis, and pregnancy experiments. RNA-Seq and molecular biology experiments were conducted to explore the role of STAT1 in regulating M1 macrophage polarization and pro-inflammatory factor secretion, thereby elucidating the underlying mechanisms of this hydrogel in treating IUA.

Results: Multi-omics data analysis and experimental validation revealed that pSTAT1 is predominantly present in M1 macrophages within the endometrium. The introduction of FA and siRNA did not alter the morphology or biological properties of the EVs. Immunofluorescence and flow cytometry demonstrated the successful preparation of M1 macrophage-targeting siRNA-loaded extracellular vesicles (siRNA@FA-EVs). Scanning electron microscopy revealed a porous network structure in all hydrogels, with no significant differences in porosity. Fourier-transform infrared spectroscopy confirmed the presence of characteristic peaks for both GelMA and SM. Lap-shear and

peeling tests demonstrated that the incorporation of SM significantly enhanced the bioadhesive properties of the hydrogel, with the 5% SM concentration exhibiting the strongest adhesion. Rheological and compression tests indicated that SM incorporation improved the mechanical properties of the hydrogel. Cell viability and CCK-8 assays confirmed the excellent biocompatibility of this hydrogel, and the release curve showed sustained and slow release of siRNA@FA-EVs from the hydrogel. In vitro experiments demonstrated that siRNA@FA-EVs/GS hydrogel inhibited STAT1 phosphorylation, thereby blocking LPS-induced M1 macrophage polarization and the release of pro-inflammatory factors, as well as the downstream differentiation of endometrial stromal cells into myofibroblasts and collagen deposition. In the rat IUA model, siRNA@FA-EVs/GS hydrogel effectively promoted endometrial and glandular repair, reduced myofibroblast activation and collagen deposition, alleviated adhesion formation, and restored fertility. Transcriptome sequencing further confirmed that siRNA@FA-EVs/GS hydrogel alleviated IUA by inhibiting STAT1 phosphorylation-mediated M1 macrophage polarization and pro-inflammatory factor release.

Conclusion: In summary, this study developed an injectable, highly adhesive hydrogel for the prevention of IUA. Upon injection into the uterine cavity, the hydrogel adheres to the injured site, preventing detachment, and continuously releases siRNA@FA-EVs. Experiments demonstrated that the hydrogel reduces M1 macrophage polarization and the release of pro-inflammatory factors by inhibiting STAT1 phosphorylation, thereby blocking the differentiation of endometrial stromal cells into myofibroblasts and collagen deposition. This process reduces adhesion formation, promotes endometrial regeneration, and restores fertility.

Key Words: Intrauterine adhesion, Macrophage polarization, Gene therapy, Extracellular vesicles, Hydrogel

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A chitosan/silk fibroin hydrogel (patch) loaded with tannic acid for promoting cardiac function repair after myocardial infarction

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Objective The irreversible damage to myocardial tissue and secondary pathological responses, such as oxidative stress, inflammation, and fibrosis, post-myocardial infarction are crucial factors contributing to the deterioration of cardiac function. In this study, based on chitosan, silk fibroin, and tannic acid, a multifunctional hydrogel myocardial patch (CS/SF/TA) was constructed. The aim was to explore its therapeutic effects on myocardial infarction (MI) and the underlying molecular mechanisms.

Methods Sprague-Dawley rats were randomly assigned to Control, MI, CS/SF, and CS/SF/TA group. The left anterior descending coronary artery of the rats was ligated to induce infarction, and then hydrogel myocardial patches were applied to the hearts of rats in the CS/SF and CS/SF/TA groups. Cardiac function was evaluated at one and four weeks after MI. Additionally, cardiac tissue and blood samples were collected to assess indicators related to myocardial inflammatory response, oxidative stress, and myocardial fibrosis.

Results Compared with the MI and CS/SF group, the CS/SF/TA hydrogel patch promotes cardiac function, delaying the process of myocardial tissue necrosis. The patch also alleviated myocardial oxidative stress damage by scavenging ROS. It also inhibited the expression of pro-inflammatory factors, thereby mitigating the inflammatory microenvironment. Histopathological results demonstrated a reduction in collagen deposition in the myocardium and approximately a 40% decrease in the fibrotic area in the patch-intervention group, indicating the inhibition of pathological myocardial remodeling. The CS/SF/TA hydrogel patch activated the PI3K-Akt signaling pathway, regulating the expression of downstream apoptosis-related proteins and angiogenic factors, and promoting myocardial cell survival and angiogenesis.

Conclusion This study reveals that the CS/SF/TA hydrogel myocardial patch promotes cardiac function repair after MI through multi-dimensional regulation of oxidative stress, inflammation, and fibrosis. This provides a novel idea and experimental basis for biomaterial-based treatment strategies for MI.

Key Words: CS/SF/TA, Hydrogel, Myocardial patch, Myocardial infarction

Acknowledgements: This work was supported by National Natural Science Foundation of China （Grant numbers 82470421）

Oxidized Dextran/Chitosan-Ibuprofen Conjugate Hydrogel for Soft Tissue Repair and Regeneration

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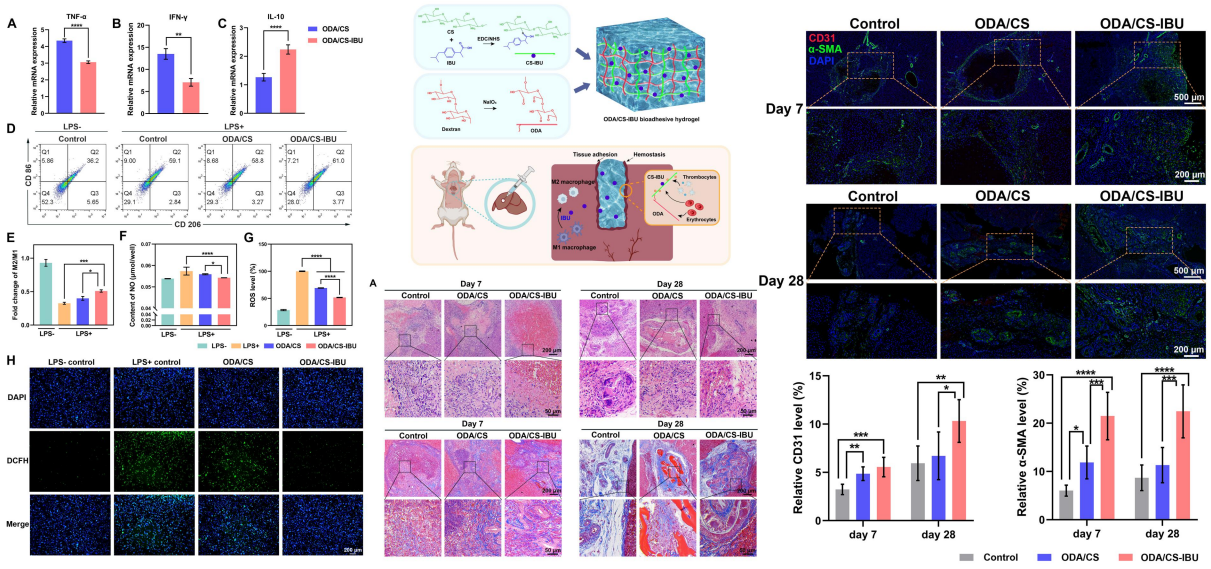
Introduction: Most of the hydrogel fail to achieve great hemostatic effect because of poor adhesion to bleeding tissues. In this work, we developed an in situ setting bioadhesive based on oxidized dextran and chitosan-ibuprofen, it has several advantages, such as rapid gelation kinetics, anti-inflammatory, antibacterial, and hemostatic capabilities. Finally, we investigated the biological performance of the bioadhesive *in vitro* and in a mouse liver partial injury model.

Research design: To generate oxidized-dextran, dextran was oxidized using periodate[1]. Besides, copolymers of CS and IBU were prepared by EDC/NHS. Upon mixing the oxidized-dextran with the CS-IBU conjugate, the ODA-CS-IBU bioadhesive hydrogel formed instantaneously.

Results & Discussion: The ODA-CS-IBU bioadhesive hydrogel has good mechanical properties and cell compatibility， and showed good antimicrobial nature against both gram positive and gram negative bacteria. *In vitro* constructed models of inflammation verified that ODA-CS-IBU hydrogel can effectively promote RAW 264.7 from M1 to M2 differentiation. Furthermore, an *in vivo* mouse liver injury model suggested that ODA-CS-IBU bioadhesive hydrogel possesses good tissue adhesion, hemostatic ability and anti-inflammatory effects.

Conclusion: The development of the bioadhesive that stops bleeding and bond the tissues well, which has good anti-inflammatory, antibacterial and antioxidant properties. In the rat liver partial resection model, the ODA/CS-IBU bioadhesive hydrogel demonstrated superior anti-inflammatory ability, contributing to robust tissue regeneration. Overall, the ODA/CS-IBU hydrogel represents a promising candidate for hemorrhage control and emergency wound care.



Key Words: bioadhesive hydrogel, chitosan-ibuprofen conjugate, hemostasis

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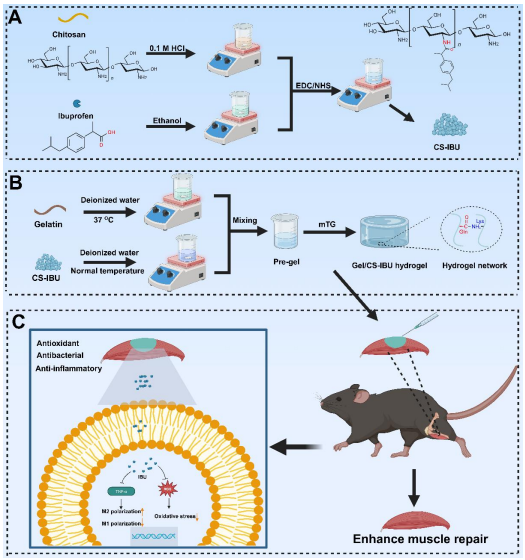
Anti-inflammatory and antibacterial hydrogel for muscle defects repair

Xiangheng Guan[1], Jinglei Wu *

Shanghai Engineering Research Center of Nano-Biomaterials and Regenerative Medicine, Department of Biomedical Engineering, Donghua University, Shanghai 201620, P. R. China

Skeletal muscle possesses a strong regenerative capacity and can repair minor injuries such as strains or contusions. However, severe trauma or surgical excision resulting in muscle volume loss (VML) exceeds the natural repair abilities of skeletal muscle, leading to significant structural and functional damage. This study develops hydrogels with anti-inflammatory and antibacterial properties for VML repair. This study mixed the prepared CS-IBU conjugate with gelatin and used transglutaminase (mTG) as a crosslinking agent to create a porous Gel/CS-IBU thermosensitive hydrogel. In in vitro characterization experiments, we found that the Gel/CS-IBU thermosensitive hydrogel exhibited enhanced mechanical properties and could adhere tightly to muscle tissue. Additionally, the hydrogel demonstrated an antibacterial rate of over 90%. In vitro, inflammatory assays showed that the Gel/CS-IBU hydrogel promoted the polarization of macrophages from M1 to M2, downregulated pro-inflammatory genes TNF-α and IL-6, and upregulated anti-inflammatory genes IL-4 and IL-10. The hydrogel also effectively scavenged reactive oxygen species (ROS) and alleviated inflammation. When applied to a mouse VML model, the Gel/CS-IBU hydrogel significantly reduced collagen deposition, alleviated the inflammatory response, and promoted muscle tissue repair, effectively repairing the defect.

KEY WORDS： Hydrogel; Chitosan; Volumetric muscle defects; Inflammation regulation; Anti-inflammatory and antibacterial



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Spiral Ganglion Cell Regeneration *via* Organ of Corti Organoids Constructed with $MgCl_2$/Gel/HA Conductive Hydrogel

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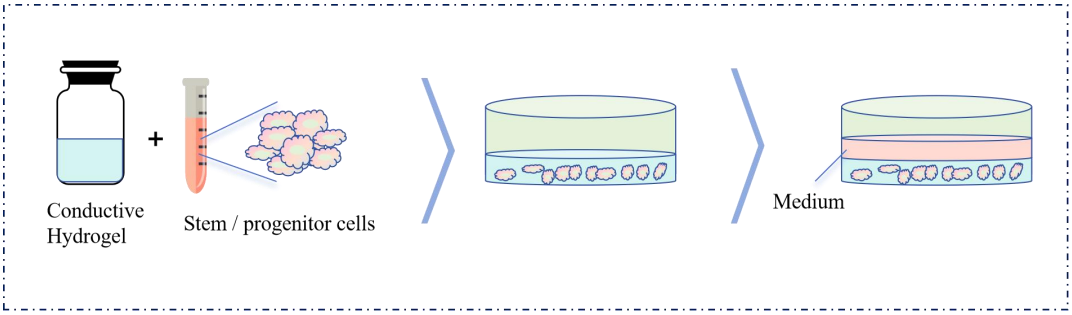
Inner ear nerve injury, often leading to irreversible hearing loss, remains a major challenge in clinical practice. Existing treatment methods for promoting inner ear nerve regeneration are quite limited. In the process of sound conduction, nerve cells and their synaptic connections play a crucial role, yet they are vulnerable to damage. In this study, a novel conductive $MgCl_2$/Gel/HA hydrogel was successfully synthesized. By using a three-dimensional culture method, inner ear organoids were constructed *in vitro*. This not only enhanced the regeneration of auditory cells but also showed potential for promoting inner ear nerve regeneration, offering a new perspective for solving inner ear nerve-related problems.



Key Words: nerve injury, Conductive Hydrogel, three-dimensional culture,inner ear

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ROS Homeostasis Protective Hydrogel Inhibiting Microglial Ferroptosis for Neuropathic Pain Alleviation and Spinal Cord Injury Repair

Zhiwen Zeng [a, *]; Lu Li [a, b], Yu Cao[b], Xiangsheng Zhang[b], Jiayi Guo [a], Jun Zhou[b, *]

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Abstract

Introduction: Traditional neuropathic pain (NP) post spinal cord injury (SCI) treatments are always limited by the chronic inflammation mediated by microglia, which hurt local neurons and hinder neural repair. The herbal compound quercetin shows great promise on SCI healing due to its antioxidant, anti-inflammatory, and anti-apoptotic effects.

Methods: Herein, an injectable protective MSQ hydrogel composed of gelatin methacryloyl, quercetin, and thiolated gelatin was prepared by UV irradiation for NP alleviation and SCI healing. The MSQ precursor solution was injected into SCI sites and crosslinked in situ to study the healing effects in SD rat SCI models.

Results: In vitro and in vivo experiments showed that the reductive thiol groups in MSQ synergize with quercetin eliminated the excess reactive oxygen species (ROS) to reconstruct ROS homeostasis and protect local tissue cells and the pharmacological effectiveness of quercetin. The MSQ hydrogels enhanced the inhibition of microglial ferroptosis, promoted anti-inflammatory microglial phenotype and accelerated axonal regeneration. Furthermore, MSQ hydrogel was proved to trigger the Slc7a11/Gpx4 pathway by activating Nrf2 in spinal microglia which was identified to regulate microglial active and phenotype.

Conclusions: MSQ hydrogel shows synergistic protection effects on local tissue cells, microglial ferroptosis inhibition, and axonal regeneration, resulting in the NP alleviation, neural repair and motor function rehabilitation. This injectable protective hydrogel provides a promising approach for NP treatment and accelerating spinal cord repair and regeneration.

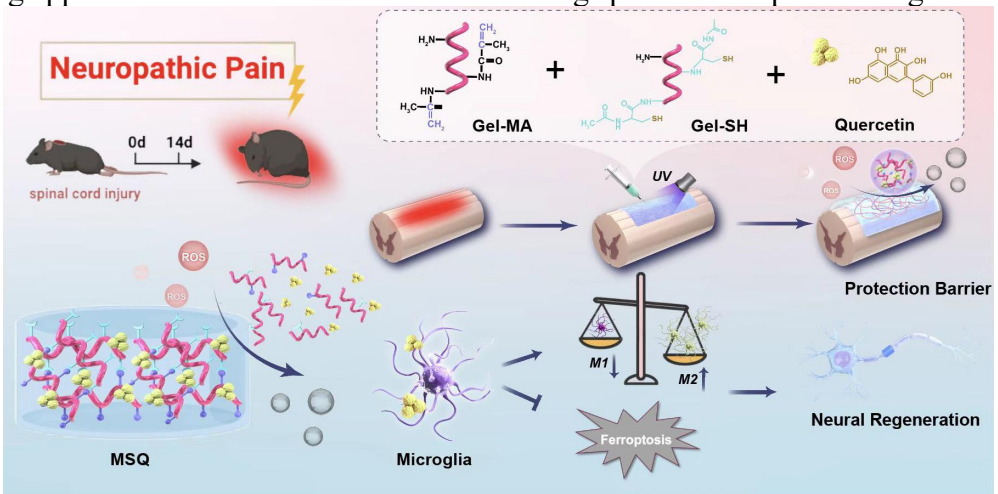

Figure1. Schemetic of the prepared protective MSQ hydrogel with antioxidation, anti-inflammation and synergistic protective effects.

Keywords: Hydrogel, quercetin, microglial ferroptosis, spinal cord injury, neuropathic pain

Acknowledgements: This research was funded by the Project of Natural Science Foundation of Guangdong Province (Grant No. 2514050000156) and the GDAS' Project of Science and Technology Development (Grant No. 2022GDASZH-2022010110). I wish to thank Doctor Zhou and his team for their help and support.

Symposia 17

Innovations in Skin-based Clinical Application

Facile Gelation of Collagen Using Green Tea Extracts for Topical Therapeutic Applications

Chixuan Liu[1], Shi Hua Tan[1], and Kun Liang[1,2]

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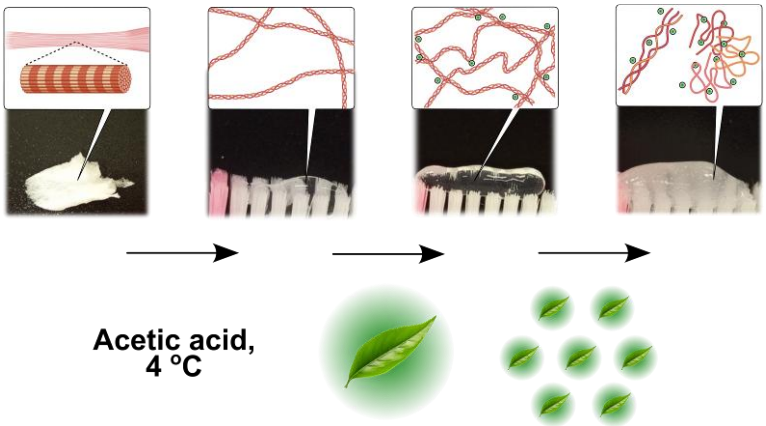
Being the primary component of the extracellular matrix, collagen is a highly favorable biomaterial for medical engineering due to its excellent biocompatibility, biodegradability, and minimal immunogenicity. Frequently, collagen materials are sourced from tissue extraction and during the application, they are processed into functional forms via gelation. However, conventional collagen gelation is a slow and tedious process that relies on gradual fibril and fiber assembly, often resulting in hydrogels with weak mechanical integrity and limited applicability in advanced medical settings. To overcome these challenges, we present a facile approach of collagen gelation using green tea extracts (GTE), a natural ingredient long recognized for its skin health benefits[1]. Upon thorough mixing with solubilized collagen, the GTE simultaneously induced the formation of a transparent and physically stable hydrogel. Our characterization results revealed that GTE crosslinked collagen by bridging individual tropocollagen triple helices, resulting in injectable, thixotropic, and processible behaviors of the collagen-GTE hydrogel. Furthermore, under excessive GTE conditions, the interactions were also observed within the internal domains of the tropocollagen units, causing partial triple helix unwinding and the appearance of micro-phase separation. Capitalizing on the hydrogel's thixotropic behavior and the established skin health benefits of both collagen and GTE[1,2], we further investigated its potential as topical therapeutics. Our results demonstrated that the hydrogel is skin-compatible, showing no irritation response when applied to *ex vivo* human skin. Additionally, it exhibited a prolonged skin-moisturizing effect compared to collagen alone. These findings highlight the promise of the GTE-collagen hydrogel as a valuable material for the development of next-generation topical therapeutics and skincare products.



Key Words: Collagen, Green Tea Therapeutics, Injectable Hydrogel, Non-covalent Crosslinking

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Innovations in Scar management

Hong Liang TEY

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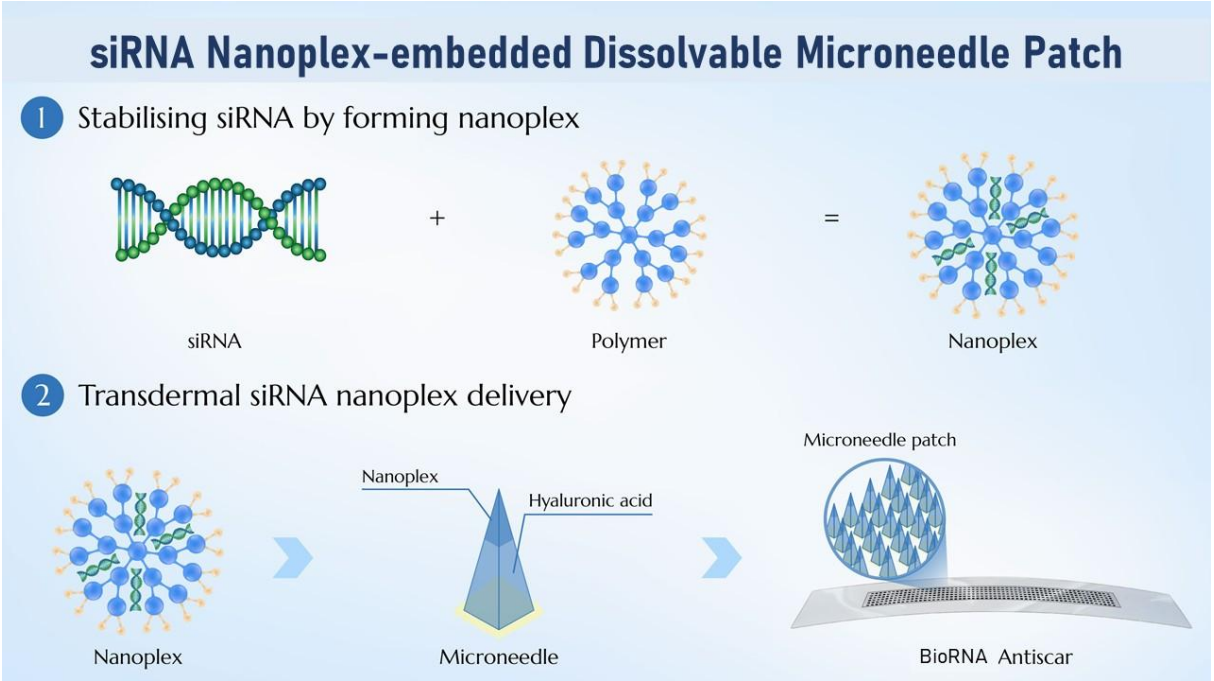
Abstract:
Existing treatments for keloids are limited, with intralesional steroid injections being the mainstay. However, many patients are unable to tolerate intralesional injection. Keloid patients often experience pain, hyperalgia and allodynia, and this corresponds with our previously finding of a trend towards a reduction in intra-epidermal nerve fibre density in keloids. Addressing this problem, we developed triamcinolone-embedded dissolvable microneedle patches. Multiple cellular and animal studies demonstrated safety and our clinical trial demonstrated that the therapy is effective in keloid patients. The therapy has been available to patients at the National Skin Centre, Singapore, and has demonstrated real-world usability, efficacy and safety.

As keloid has long chronicity, to enhance safety for prolong use, we further developed RNA therapeutics-embedded dissolving microneedles to provide highly precise targeted therapy. This involves siRNA binding to mRNA, inhibiting SPARC protein translation and reducing formation of collagen bundles. The siRNA is complexed in a nanoplex, safeguarding it from degradation and facilitating fibroblast receptor binding. Administered through dissolvable microneedles, this method ensures precise delivery 'to the right cells in the right organ,' overcoming a key challenge in RNA therapeutics. Cellular, animal, and clinical studies demonstrated safety and efficacy in significantly reducing scar tissue formation. As there is no cure for keloids, prevention is key. The siRNA-microneedle patch has been commercialised and has been used for preventing excessive scar tissue formation post-skin surgery.

Expansion and recurrence after treatment is the hallmark of keloids. To address upstream pathogenetic factors, we have further embedded a siRNA down-regulating inflammatory cytokines, in addition to siSPARC inhibiting collagen formation. Our clinical trial has demonstrated feasibility of this approach and opens the field of multi-targeted treatment in a single product for enhanced management of complex diseases.



Graphic legend: Our nano-polymer protects the siRNA from degradation by RNAase ubiquitous in the environment and tissues. It also carries ligands that bind to receptors on the target cells – fibroblasts in scars. The nanoplex is delivered across the skin barrier using dissolvable microneedles comprised of hyaluronic acid. Suffers apply the adhesive patch over night to prevent and reduce raised scars, including hypertrophic scars and keloids.

Key Words: keloid, hypertrophic, siRNA, microneedles, dissolvable

Acknowledgements:
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In Vivo NMR Relaxation Study of Human Skin

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The skin is the largest organ of the human body and has the most extensive surface area in contact with the environment. It serves multiple functions: protecting internal organs, regulating body temperature, and synthesizing vitamin D. The condition of the skin reflects the overall state of the body. Low-field NMR equipped with a single-sided probe, the NMR-MOUSE (Mobile Universal Surface Explorer), is well-suited for studying the skin [1]. The 1H NMR relaxation of water content in the skin, measured using the CPMG technique, can be employed to monitor the behavior of water in different layers of the skin. Due to the high field gradient of the MOUSE device, diffusion significantly influences the relaxation rate and may even dominate it. The classical Hahn-echo experiment is particularly sensitive to diffusion effects compared to CPMG due to its longer echo times (Figure 1).

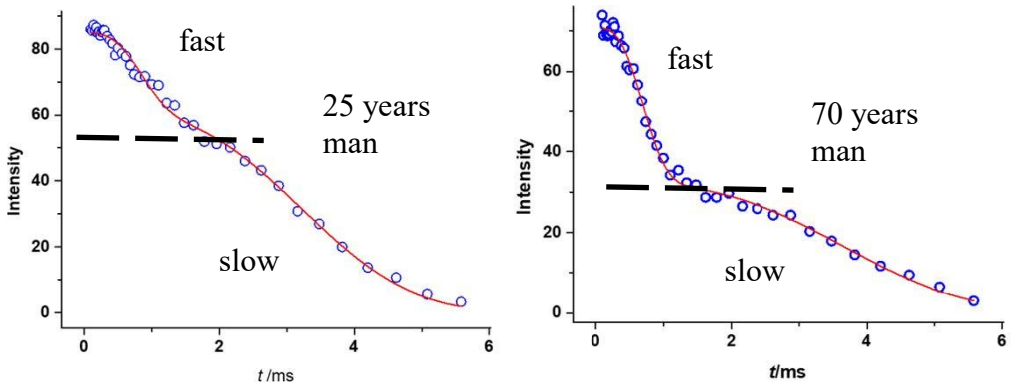

Figure 1. The Hahn echo *in vivo* experiment on the skin of the lower part of forearm.

Figure 1 illustrates that two types of water can be identified at a depth of 3 mm in the studied samples. The amount of faster-moving water is higher in older individuals, and the fitted diffusion coefficient is approximately twice as large. This observation aligns with expectations since collagen and hyaluronic acid content decreases with age. Water mobility is primarily determined by its bonding to collagen.

It should be noted that the hydration properties of human skin are not exclusively determined by age. They also depend on factors such as gender, skincare habits, environmental conditions, workplace exposure, and overall skin health. Systematic investigations and the creation of a comprehensive database will aid in the medical characterization of human skin. The described experiment meets standard diagnostic requirements: it is painless, non-destructive, and takes less than half an hour.

Key Words: human skin, in vivo study, water diffusion, low-field NMR, NMR-MOUSE,

Acknowledgements: This work financed by the Hungarian National Research, Development and Innovation Office (NKFIH) in frame of grant no.: K 131989

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Human skin microbiome sampling based on a transepidermal microprojection array for clinical applications

Kun Liang[1,2], Jia Min Loh[1], Larissa Lim[2], Cheryl Leong[2], Thomas Dawson[2] and Hong Liang Tey[1,3]

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Introduction & Research design

The skin microbiome plays an important role in skin health and disease. Most of current human skin microbiome sampling have been performed using tools such as swab, tape strip and scrape, which collect microbes solely on the skin surface. With the emergence of studies showing that the distribution and abundance of skin microbes varies with skin depth, there has been increasing recognition of the gap in knowledge of microbiota colonization in deeper skin layers. However, apart from the invasive skin biopsy being the only method to sample deeper skin microbiome, there are limited means to collect such samples. Herein, we developed a simple and minimally-invasive sampling tool with a depth component – a transepidermal microprojection array (MPA) for microbiome sampling [1]. We hypothesize that the MPA-mediated transepidermal sampling will potentially facilitate clinical diagnosis of skin microbial infections.

Main results & Discussion

The MPA was fabricated by customizable computer-aided design and 3D printing and systematically optimized for the microbial extraction efficiency and skin penetration depth [1,2]. In a proof-of-concept trial on human subjects, we investigated the microbial extraction efficacy and the downstream metagenome sequencing quantification of the MPA samples in comparison with the conventional swab and tape strip. We found that MPA was comparable in sensitivity to swab and superior to tape strip, especially for non-standard skin surfaces. In particular, for fungi sampling, MPA showed the highest species diversity. In a clinical study on patients with fungal infections, we demonstrated the utility of MPA to collect the etiological microbes to help diagnose fungal infections.

Conclusion

We developed a novel approach for the minimally-invasive sampling of human skin microbiome in the deeper sub-epidermal regions. We envision that this can help address the gaps in our knowledge of microbial colonization across the skin with potential clinical use in diagnosis of microbial infections.

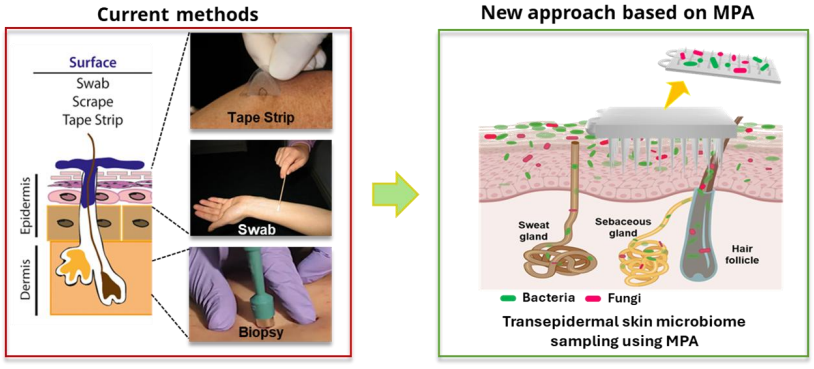

Figure 1. New approach of transepidermal sampling of skin microbiome based on microprojection array (MPA)

Key Words: skin microbiome sampling, microprojection array, 3D printing, fungal infections

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Antibiotic-Free Nanofibrous Scaffolds for Enhanced Healing of Diabetic Wounds

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Diabetic ulcers present a significant clinical challenge due to impaired healing processes and heightened risk of infection, requiring innovative specialized dressings. Here, we present our development of a tunable dressing composed of aligned nanofibrous scaffolds incorporating an antimicrobial polymer ε-polylysine (ε-PL). The scaffold design mimics the structure of native skin extracellular matrix, aiming to support cell migration and tissue remodeling. Aligned nanofibrous scaffolds were prepared by electrospinning biocompatible polymers, with ε-PL uniformly integrated to provide intrinsic antibacterial properties. *In vitro* assays demonstrated that nanofiber alignment significantly enhanced the directional motility of human dermal fibroblasts and keratinocytes, which are critical for effective wound closure. Additionally, ε-PL incorporation resulted in robust bactericidal activity against both Gram-positive and Gram-negative pathogens. *In vivo* evaluation using full-thickness wound models in both diabetic mice and porcine skin confirmed accelerated wound healing, reduced inflammation, and improved re-epithelialization, with outcomes comparable to or better than commercial silver-based dressings. These findings highlight the multi-functionality of the ε-PL nanofibrous scaffolds in promoting wound repair while mitigating infection risk. The innovative dressing prototype thus provides an antibiotic-free solution for treating diabetic wounds and potentially managing other skin injuries.

Key Words: Broad-spectrum antimicrobial, Cationic polymers, Dressing, Skin wounds.

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Diffuse Speckle Pulsatile Flowmetry (DSPF) for Skin Microcirculation Assessment: A Novel Approach for Diabetic Foot Ulcer Monitoring and Peripheral Vascular Disease Screening

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Skin microcirculation plays a critical role in maintaining tissue viability and wound healing, particularly in conditions like diabetic foot ulcers (DFU) where compromised blood flow leads to chronic non-healing wounds and increased amputation risk. We introduce Diffuse Speckle Pulsatile Flowmetry (DSPF) [1], a high-speed, noninvasive optical technique capable of measuring deep tissue pulsatile blood flow with subcutaneous penetration up to 20 mm. DSPF leverages multimode fiber-based detection to achieve a high temporal resolution (300 Hz), providing real-time microvascular flow assessment [2].

In this study, we adapt DSPF for skin perfusion monitoring in DFU, utilizing a new Tissue Perfusion Index (TPI_{DSPF}), derived from frequency-domain analysis of the pulsatile flow waveform. A clinical investigation in diabetic patients demonstrated that TPI_{DSPF} correlates strongly with standard perfusion metrics (transcutaneous oxygen pressure and toe-brachial index), outperforming existing methods in detecting ischemia. Notably, DSPF successfully distinguished early-stage perfusion impairments, which are often undetected using conventional techniques.

Our initial validation in peripheral artery disease (PAD) screening among diabetes patients may provide new opportunities in population health monitoring and screening in ageing society. By bridging microvascular dysfunction assessment in PAD and DFU, DSPF emerges as a powerful tool for skin technology innovations, with potential implications in regenerative medicine, wound care, and non-invasive vascular diagnostics.

Key Words: diffuse speckle, blood flow, diabetic foot ulcer, peripheral artery disease

Acknowledgements: We acknowledge the funding support by Biomedical Engineering Programme C221318003, and the Gap Project I22AEAG006 from A*STAR.

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Symposia 18

Innovative Biomaterials for Organ Models and Tissue Repair

Is Subchondral Bone Remodeling a Result or a Contributor to OA Progression?

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Introduction: Osteoarthritis (OA) is a multifactorial joint disorder characterized by cartilage degradation, synovial inflammation, and subchondral bone remodeling. While subchondral bone alterations—such as sclerosis, microcrack formation, and angiogenesis—are well-documented in OA, their role in disease progression remains contentious [1]. This paper explores the pivotal question: Is subchondral bone remodeling a secondary consequence of cartilage damage or an active contributor to OA pathogenesis?

Materials & Methodology: Femoral heads from hip arthroplasty for primary osteoarthritis (n=7) and femoral neck fracture (n=6; non-OA controls) cases were collected and characterized with respect to spatial microstructural and chemical composition changes. Principal component analysis (PCA), a data reduction method, was employed to assess differences between OA and non-OA samples, and the spatial relationship between CLS and subchondral bone changes.

Results and Discussion: The examination of the human OA tissues demonstrates that subchondral bone remodeling may precede cartilage degeneration, driven by aberrant osteoclast-osteoblast activity, pro-inflammatory cytokines, and dysregulated signaling pathways (e.g., Wnt/β-catenin, TGF-β), as well as microstructure and chemical composition changes. The OA-related changes in subchondral plate architecture were correlated with CLS in all quadrants, especially in the higher weight-bearing regions of the femoral head. Greater articular cartilage deterioration in OA was regionally-linked with lower BV/TV, TMD and thickness, and greater BS/BV and porosity in the subchondral plate; and with thinner, less separated trabeculae with greater TMD and BS/BV in the trabecular bone. These findings suggest that impairment of subchondral bone microstructure in early stage of OA is more readily discernible in the cortical plate and that morphological characterisation of the femoral head bone microstructure may allow for earlier OA diagnosis and monitoring of progression.

Conclusion: The authors believe that these processes could exacerbate joint instability, alter load distribution, and promote catabolic cartilage responses through biochemical and biological crosstalk. Conversely, cartilage-derived factors may reciprocally drive bone remodeling, highlighting a bidirectional relationship. Resolving this debate requires longitudinal studies integrating advanced imaging, biomechanical modeling, and molecular profiling to delineate temporal and causal relationships. Clarifying the role of subchondral bone in OA could unlock novel strategies for early intervention and disease modification, shifting the paradigm from symptom management to structural preservation

Key Words: Osteoarthritis, cartilage, scaffold, subchondral bone

Acknowledgements: This work is funded by Innovate UK (grant no: A02872) and the International Science & Technology Cooperation Program of Hainan Province (grant No. GHYF2022001).

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Chemically Modified Silk Fibroin for Regenerative Medicine

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Introduction: Silk fibroin derived from the domesticated silkworm *Bombyx mori* is a protein-based biopolymer with low immunogenicity, intrinsic biodegradability, and tunable mechanical properties, showing great potential in biomedical applications. However, natural silk fibroin lacks bioactivity and functionalities. With chemical modifications, the primary structure of silk fibroin can be modified to achieve desired functions, enabling the expanded generation of new silk-based biomaterials. Here, we demonstrated chemically modified silk fibroin materials with great potential in regenerative medicine and tissue engineering.

Research design: The serine residues in regenerated silk fibroin are chemically modified with succinic anhydride in dimethylsulfoxide (DMSO) to obtain carboxylated silk fibroin, named silk acid (SA). The molecular structures, physical properties, and biological properties of the SA materials were characterized by NMR spectroscopy, *in vitro* enzymatic degradation and cell culture, histological staining, and immunohistochemical staining. An *in vivo* implantation study was performed to investigate the biocompatibility and controlled *in vivo* biodegradability of SA materials. Furthermore, derivatives of SA materials were developed to enhance the bioactivities in various biomedical applications.

Main results & Discussion: A green and efficient method with scaling-up potential was demonstrated to achieve controlled carboxylation of regenerated silk fibroin, creating silk acid (SA). Compared to regenerated silk fibroin, The SA materials show tunable hydrophilicity and *in vitro* enzymatic degradation properties at different carboxylation degrees (CDs). Subcutaneous implantation in mice for up to one month reveals that the SA materials with a high CD enhance degradation while causing a mild foreign-body response, including a low inflammatory response and reduced fibrotic encapsulation. Immunofluorescence analysis further indicates that the SA materials show pro-angiogenesis properties and promote M2-type macrophage polarization to facilitate tissue regeneration.

Conclusions: Novel silk-based materials based on chemically modified silk fibroin are demonstrated with great promise in biomedical applications such as tissue regeneration and 3D cell culture.

Key Words: Silk fibroin, chemical modification, tissue regeneration, regenerative medicine

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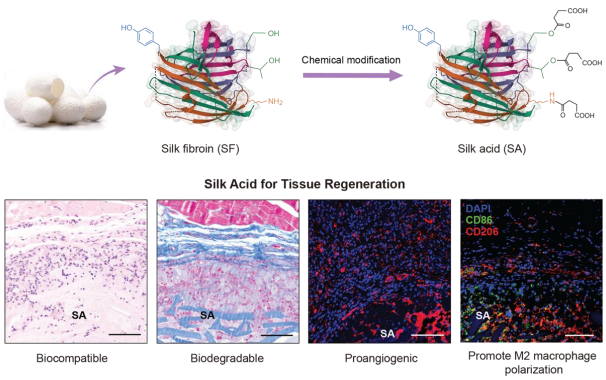

Abstract graphic

Wet-Spun Biomimetic Fibers for Enhanced Spinal Cord Injury Repair

Keni Yang[1], Yun Chu[1], Haitao Zhao[1], Lin Qian[1], Yanyan Chen[1*], Jianwu Dai[1*]

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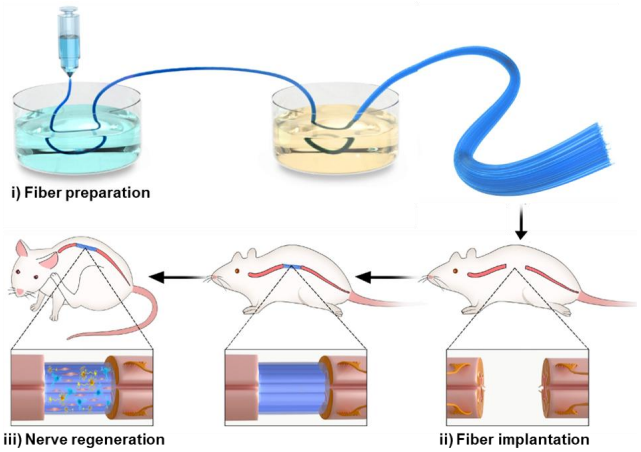
Spinal cord injury (SCI) is one of the most devastating diseases, interrupting the neural networks that bridge the brain and body and leading to motor and sensory dysfunctions and paralysis below the lesion. While biomaterials hold great promise for SCI repair, many lack directional cues to guide neural cell activity and bioactive components to modulate cellular response, limiting their therapeutic potential. Within this context, we have developed a series of functional fibers using natural polymers via a facile wet-spinning technique, aiming to enhance SCI intervention efficacy. These include a dual-network collagen fiber featuring microscale guidance cues, comparable mechanical strength to native spinal cord tissue and tunable porosity. This fiber activates mechanotransduction signaling pathways in neural stem cells (NSCs), promoting their adhesion, alignment and differentiation, ultimately improving SCI repair. Building on this design, we loaded baicalein, a clinically approved drug we identified to promote neuronal differentiation of NSCs, in the collagen matrix. The baicalein-functionalized collagen scaffold enables sustained drug release and facilitates neurogenesis both *in vitro* and in SCI tissues. Furthermore, a micron-sized fiber with parallel nanoscale grooves on the surface was developed, using alginate for its rapid crosslinking property, with gelatin conjugated to the alginate and calcium crystallites deposited to enhance biostability and mechanical property. These hierarchically oriented fibers mimicking spinal cord architecture not only align neural cell distribution but also promote axonal outgrowth along the fiber axis. When implanted in SCI rats, they significantly facilitate motor functional recovery and tissue integration, and markedly improve neural regeneration and neurite extension at the injured sites. Together, these studies present effective strategies for fabricating biomimetic fibers for SCI repair and more importantly, highlight the critical role of oriented biomaterial structures in guiding neural cell behavior and promoting functional recovery.



Schematic of wet-spun biomimetic fibers implanted in rat lesion sites to promote SCI repair.

Key Words: Wet spinning, Biomimetic fibers, Nerve regeneration, Spinal cord injury

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Creating Biomimetic Scaffolds for In Vitro Organ Models and In Vivo Tissue Regeneration

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Scaffold biomaterials play a critical role in the engineering of *in vitro* tissue/organ models and the regeneration of *in vivo* damaged tissues by facilitating cell and tissue growth [1-3]. An effective strategy for developing optimal scaffolds is to mimic the natural extracellular matrix (ECM) which is a 3D nanofibrous network with sufficient porosity or pore size for the growth of cells and tissues [1, 2]. To date, many efforts have been made to create biomimetic materials. However, recapitulating the structure and function of the natural ECM remains a significant challenge.

Our previous study originally discovered that ice crystals and softer matter can shape one another [1]. Based on this discovery, we deliver a self-assembly technology platform for developing biomimetic scaffolds that can recapitulate the natural ECM's hierarchical structure and function (Fig. 1). Our findings demonstrate that these developed biomimetic architectures can direct the behavior and function of cells and the growth of tissues, thereby facilitating the engineering of tissue and organ models *in vitro* and the regenerative repair of damaged tissues *in vivo*.

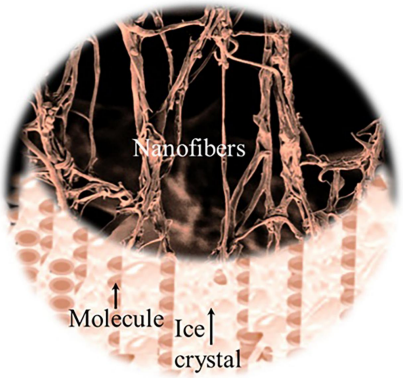

Fig. 1. Growth of ice crystals directing self-assembly of molecules to nanofibrous scaffolds.

Key Words: Biomimetic architecture, nanofiber, self-assembly, organ models, tissue regeneration

Acknowledgements: The Australian Research Council (ARC) is acknowledged for its support through a Future Fellowship project (FT230100220).

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AI-Enabled Wound Image Analysis for Diabetic Limb Salvage: From Clinical Need to Explainable Intelligence

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Diabetic foot ulcers (DFUs) represent a growing global burden, with high rates of morbidity, limb loss, and healthcare expenditure. In Singapore, our multidisciplinary care model—DEFINITE (Diabetic Foot in Primary and Tertiary) Care—has demonstrated improved amputation-free survival and cost-effectiveness, yet gaps persist in wound surveillance and timely intervention [1-2]. To address this, we developed an explainable artificial intelligence (AI) model trained on over 18,000 vascular wound images, capable of classifying wound types, segmenting wound areas, and quantifying healing progression.

Using convolutional neural networks such as DenseNet and ResNet architectures, and explainability tools like GradCAM and SHAP, the AI achieved AUROC scores of 0.75–0.99 for classification and segmentation tasks. Explainability scores ranged from 24% to 90%, enabling greater clinical trust [3]. The AI was integrated into a mobile platform to support both clinician workflows and patient-facing applications.

In the next three years, we will validate the tool through prospective studies in outpatient DFU clinics, and will extend its use in community-based care models, combining AI-generated wound healing reports with telemonitoring and patient activation strategies. This system empowers patients and caregivers with real-time wound insights and alerts clinicians to deterioration events—supporting earlier, targeted interventions.

In conclusion, the integration of explainable AI into diabetic wound care demonstrates a scalable pathway from data to bedside, and from tertiary care to the community—reshaping diabetic limb salvage through intelligent, patient-centric design.

Key Words: diabetic limb salvage, multi-disciplinary team, artificial intelligence, wound imaging

Acknowledgements: NMRC Research Training Fellowship, NMRC HPHSR Clinician Scientist Award, NHG Population Health Fund

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Symposia 19

Nano and Microtechnologies for Drug Delivery and Tissue Regeneration

Emerging New Forms of Electrospun Nanofibers for Tissue Regeneration

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Introduction

Over the last two decades, electrospinning has become a key nanotechnology for fabricating nanofiber materials used in a wide range of biomedical applications. Notably, therapeutic and cell-loaded nanofiber scaffolds have been extensively studied for drug delivery, wound healing, and tissue repair and regeneration. However, conventional nanofiber scaffolds often face limitations such as low porosity, small pore size, lack of injectability, and limited spatial control. As a result, significant efforts have been directed toward developing novel forms of nanofiber materials to overcome these challenges.

Research Design

Different forms of electrospun nanofibers were developed by electrospinning, gas-foaming cryocutting, freeze-casting, and/or crosslinking. These materials were tested in various biomedical applications.

Results and Discussion

3D expanded nanofiber scaffolds with various shapes and controlled fiber alignment, nanofiber microspheres, nanofiber aerogels, and hybrid aerogels were successfully generated [1-3]. These materials were demonstrated highly effective in managing hemorrhage and repairing bone defects.

Conclusion

We have fabricated new forms of electrospun nanofiber materials including expanded 3D nanofiber scaffolds, nanofiber aerogels, hybrid aerogels, and nanofiber microspheres for various biomedical applications.

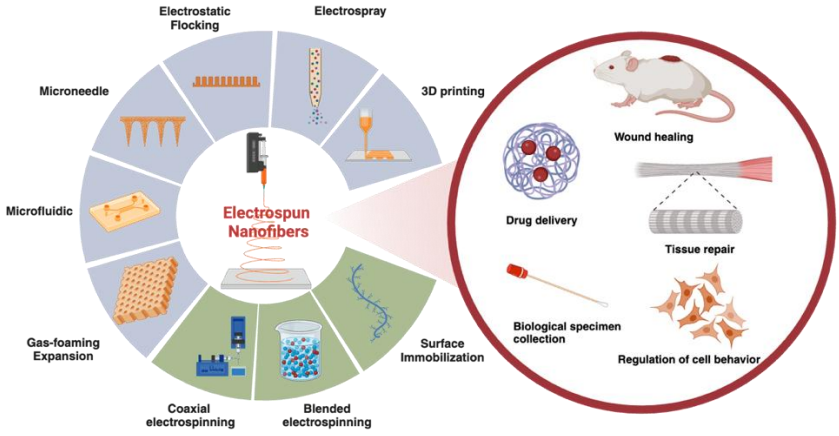

Figure 1. Electrospun nanofiber materials incorporated with bioactive materials via surface immobilization or encapsulation and integrated with other technologies for biomedical applications.

Key Words: Electrospun Nanofibers, Gas-foaming, Expansion, Tissue Regeneration

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3D Hierarchically Aligned Nanofiber Scaffolds Promote in Situ Tissue Regeneration Through Enhancing Collective Cell Migration

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Abstract

Recruiting cells from surrounding tissue to the defect site is a crucial first step in the process of in situ tissue regeneration. In our previous studies, we have developed strategies that integrate electrospinning, weaving, thermal fixation, and modified gas-foaming technologies to fabricate 3D hierarchically aligned nanofiber scaffolds. These scaffolds exhibit high porosity, controlled fiber alignment, and diverse configurations (uniaxial, bi-directional, radial, and gradient alignments), creating effective 'cell highways' for promoting collective cell migration. Both in vitro and in vivo, the highly porous and directionally arranged 3D nanofiber scaffolds markedly enhance cell migration, accelerating the reconstruction of defective tissues. Moreover, single-cell sequencing and spatial transcription revealed that 3D-aligned nanofiber scaffolds can recruit more endothelial cells and fibroblasts and fewer immune cells compared to traditional non-nanoscale scaffolds. Compared with random 3D short nanofiber scaffold, the 3D aligned nanofiber scaffolds could recruit more endothelial cells, DCs, T cells, and neutrophils. Furthermore, in the granulation tissue induced by the 3D aligned nanofiber scaffold, the extracellular matrix genes Frem1 and collagen 15 were highly expressed. This is the interaction between the extracellular matrix and cells that traditional 2D studies have failed to reveal. The researches on 3D aligned nanofiber scaffolds promoting collective cell migration can provide more theoretical guidance for the research and development of the next generation of wound healing products.

Key Words: 3D aligned nanofiber scaffold, Tissue regeneration, Collective cell migration

Keratin-polyphenol bioadhesives for soft tissue attachment to transcutaneous bone-anchored metallic prostheses

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Introduction: Intraosseous transcutaneous amputation prostheses are bone-anchored metallic implants that protrude through the skin to extracorporeal knee fixtures. While titanium osseointegration is excellent, its soft tissue integration is impeded by skin epidermal downgrowth, peri-implantitis and infection. Therefore, we propose a skin-compatible bioadhesive for peri-implant soft tissue sealing [1].

Research Design and Methodology: To formulate an external bioadhesive, reduced keratins extracted from human hair and chicken feathers were coupled with polyphenols (dopamine, tannic acid and quercetin). A freeze-thaw process induced gelation via disulfide recombination was employed. Rheology and adhesion strength of the injectable glues when applied between porcine intestinal mucosa and titanium sheets were characterized. Further, relevant skin and immune cell types were used to evaluate skin compatibility and anti-inflammatory activity of the developed bioglues.

Main Results and Discussion: Adhesion strength by lap shear test revealed higher glue strength of human hair keratin (HHK) than chicken feather keratin (CFK) when applied between porcine mucosa and titanium. Both HHK and CFK exhibited improved glue strength with polyphenol addition, especially tannic acid. Adhesion test data suggests the higher molecular weight (40–60 kDa) of HHK contributed to its superior glue strength than CFK (8 – 10 kDa), despite a 2-fold greater thiol content in CFK than HHK. Rheological characterization divulged stiffer CFK gels with ~10-fold higher storage moduli than HHK commensurate with their thiol content. All the gels (HHK ± Polyphenol and CFK ± Polyphenol) were injectable into aqueous media and dry surfaces, suggesting their potential use as bioinks for Bioprinting. The glue formulations coated on titanium supported skin cell adhesion (*HaCaT* – immortalized human epidermal keratinocytes and *E. Derm* – equine dermal fibroblasts). Antioxidant activity of the glues was evidenced by DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging. Anti-inflammatory activity is being studied using RAW 264.7 murine macrophages.

Conclusion: Our reduced keratin-polyphenol bioadhesive formulations can help promote peri-implant soft tissue sealing around metallic abutments.

Key Words: Percutaneous bone-anchored prosthesis, Titanium, Keratin-polyphenol bioadhesives, Epidermal down growth, Peri-implant sealing

Acknowledgements: Funding from the Board of Research in Nuclear Sciences (BRNS), Govt. of India and IIT Madras New Faculty Ignition Grant (NFIG)

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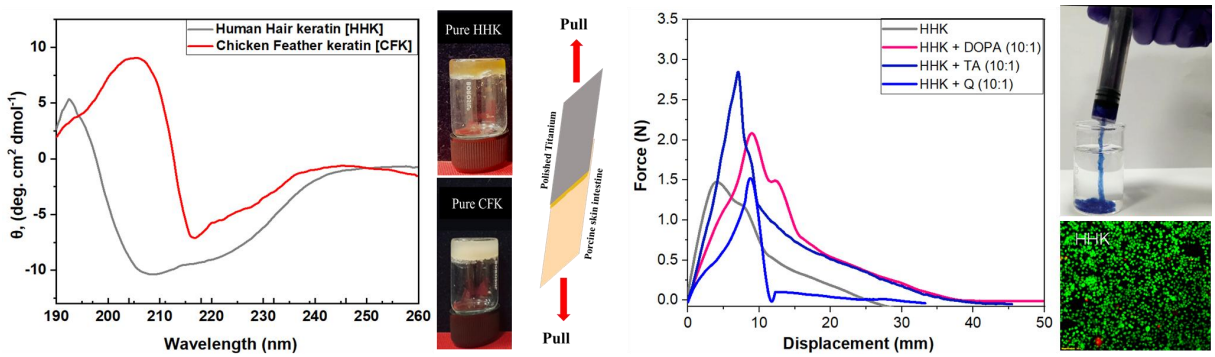

Microneedle Patch for Improved Heart Failure Outcomes in Post Myocardial Infarction Rats

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Introduction: After myocardial infarction, the heart undergoes adverse remodeling characterized by a series of pathological changes, including inflammation, apoptosis, fibrosis, and hypertrophy. In addition to cardiac catheter-based re-establishment of blood flow, patients typically receive multiple medications that aim to address these different mechanisms underlying left ventricular remodeling. The current study aims to establish a versatile multi-drug delivery platform for the controlled and sequential delivery of multiple therapeutic agents in a single treatment. **Research design:** We generated a microcapped microneedle patch carrying methylprednisolone, interleukin-10, and vascular endothelial growth factor. In vitro characterization demonstrated a time-sequenced release pattern of these drug: methylprednisolone for the first 3 days, interleukin-10 from day 1 to 15, and vascular endothelial growth factor from day 3 to 25. The therapeutic effects of the microneedle patch were evaluated in a rat model of acute myocardial infarction induced by permanent ligation of left anterior descending coronary artery. Heart function was measured using trans-thoracic echocardiography. Heart inflammation, apoptosis, hypertrophy and angiogenesis were evaluated using histology. **Main results:** Our data indicated that, at 28 days after patch transplantation, animals receiving the microneedle patch with sequential release of these three agents showed reduced inflammation, apoptosis and cardiac hypertrophy compared to the animals receiving control patch without sequential release of these agents, which is associated with the improved angiogenesis and heart function. **Conclusions:** The microneedle patch can be utilized to deliver multiple therapeutic agents in a controlled and sequential manner that aligns with the pathological phases following myocardial infarction.

Key Words: myocardial infarction, heart failure, rat, microneedle, patch

Symposia 20

Nanomedicine and Nanobiotechnology

Mesoporous copper sulfide-based nanocomposites for non-oxygen dependent free radicals-assisted photothermal therapy of uveal melanoma

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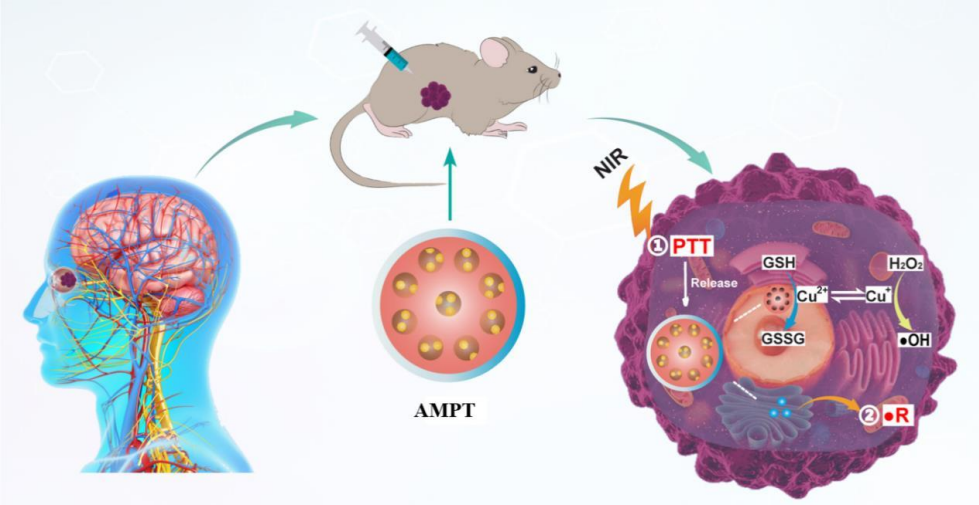
Uveal melanoma (UM) is an ocular cancer predominantly affecting adults, characterized by challenging diagnostic outcomes. This research endeavors to develop an innovative multifunctional nanocomposite system sensitive to near-infrared (NIR) radiation, serving as both a non-oxygen free-radical generator and a photothermal agent. The designed system combines azobis isobutyl imidazoline hydrochloride (AIBI) with mesoporous copper sulfide (MCuS) nanoparticles. MCuS harnesses NIR laser energy to induce photothermal therapy, converting light energy into heat to destroy cancer cells. Simultaneously, AIBI is activated by the NIR laser to produce alkyl radicals, which induce DNA damage in remaining cancer cells. This distinctive feature equips the designed system to selectively eliminate cancers in the hypoxic tumor microenvironment. MCuS is also beneficial to scavenge the overexpressed glutathione (GSH) in the tumor microenvironment. GSH generally consumes free radicals and hiders the PDT effect. To enhance control over AIBI release in cancer cells, 1-tetradecyl alcohol (TD), a phase-changing material, was introduced onto the surface of MCuS nanoparticles to create the final AMPT nanoparticle system. In vitro and in vivo experiments confirm the remarkable anti-tumor efficacy of AMPT. Notably, the study introduces an orthotopic tumor model for UM, demonstrating the feasibility of precise and effective targeted treatment within the ocular system.



Key Words: Uveal melanoma, mesoporous copper sulfide, alkyl radicals, photothermal treatment, orthotopic models for ocular tumors.

Acknowledgements: This research received financial support from the Key R&D Program of Zhejiang Province (2021C04019), and the National Natural Science Foundation of China (82202354 and U20A20338).

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Supramolecular Cell Engineering for Targeted Therapy

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Cells are a basic unit of living organisms and using them as drug carriers or therapeutics has unique advantages. During the past several years, we have developed a unique "supramolecular cell engineering" approach where nanomedicines or biomaterials are self-assembled either extracellularly or intracellularly via artificial host-guest interactions, to anchor nanomedicine or biomaterials either on the surface of, or inside, the cells for targeted delivery to specific tissues, e.g. driven by the inflammatory tropism of immune cells.[1] We show that the supramolecularly engineered cells may efficiently deliver medicine to disease tissues and effectively treat several diseases including acute pneumonia, cardiovascular diseases and solid tumors.[2] We also show that intracellularly gelated macrophage may function as "cell sponge" to absorb inflammatory cytokines, endotoxins and even bacteria, to effectively fight against infectious diseases.[3]

Key Words: targeted delivery; cell engineering; nanomedicine; supramolecular chemistry

Acknowledgements: The Science and Technology Development Fund of Macau SAR (0127/2024/RIA2, 0086/2022/A2, 0047/2023/AMJ) and Taihu Innovation Scheme of Jiangyin Hi-tech Industrial Development Zone (JOIND) (EF2025-00001-SKL-QRCM).

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Activatable nano aggregation systems for tumor diagnosis and treatment

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Malignant tumor (cancer) has become an important killer endangering national health. In the process of tumor treatment, there are widespread problems such as poor targeting and low concentration of drugs in the tumor area, which not only affect the therapeutic effect, but also bring great systemic toxic side effects. Therefore, how to improve the concentration and residence time of nanocatalytic drugs at tumor sites, and to clarify the biological mechanism of nanocatalytic drugs on normal tissues and tumor tissues are the key problems to be solved. In view of this, we proposed to construct a nanoaggregation system activated in situ by tumor region for tumor treatment, and utilize the high expression characteristics of reactive oxygen species unique to tumor environment and mild covalent chemical crosslinking segment to achieve specific enrichment of nanomaterials at tumor sites [1], further combining detection and treatment (Figure 1). Responsive nanomaterials and prodrug systems that can be specifically activated by reactive oxygen species in the tumor microenvironment have been developed to achieve efficient targeted treatment of in-situ tumors and metastases [2]. This activation strategy has also been used to effectively treat other diseases related to the concentration of reactive oxygen species or metal ions, such as Wilson's disease [3].

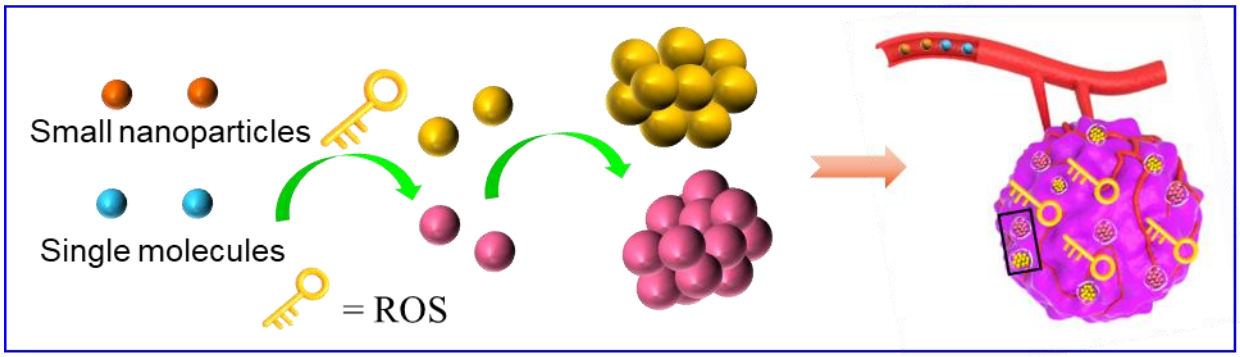

Figure 1. Schematic description of activatable nano aggregation systems for tumor diagnosis and treatment

Key Words: tumor, aggregation, active, drug release

Acknowledgements: We gratefully acknowledge the financial support from NNSFC (22371038, 22177019)

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Immunomodulatory hydrogel loaded with curcumin and tannic acid assembled nanoparticles for radiation-induced dermatitis repair

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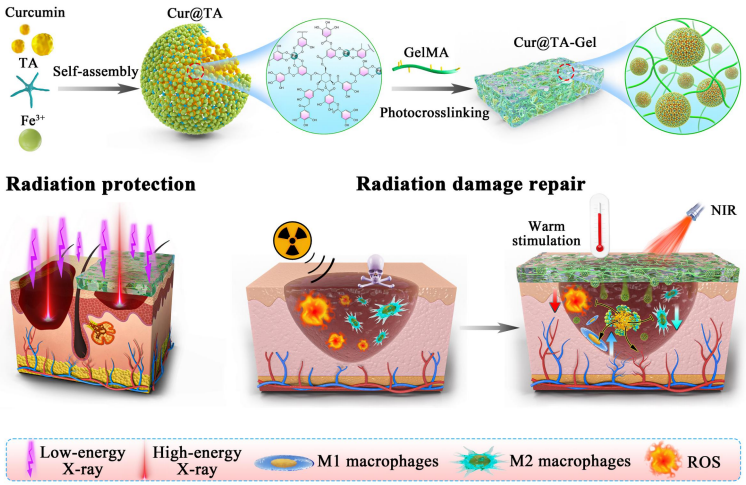
Radiation dermatitis, as a major side effect of radiotherapy, is a form of skin injury linked to the production of reactive oxygen species (ROS). Herein, we present a nanohybrid hydrogel patch composed with natural-derived substances. The patch possesses dual functionalities of chemically scavenging ROS and physically absorbing radiation, thereby alleviating radiation damage. Curcumin@tannic acid (Cur@TA) nanoparticles are synthesized through spontaneous coordination of TA and iron ions (Fe^{3+}), enabling the encapsulation of Cur. The nanoparticles are then loaded into methacrylate gelatin (GelMA) hydrogel patches, which endow the hydrogel with tissue adhesion as well as photothermal properties. Simultaneously, the patch exhibits powerful ROS scavenging capability and promotes M2 polarization of macrophages. Additionally, the high-water content of the GelMA hydrogel enables physical absorption of low-energy X-rays, providing radiation shielding. Based on these characteristics, we have demonstrated the augmented therapeutic efficacy of the hydrogel patch loaded with Cur@TA nanoparticles in the mouse model of radiation dermatitis. Our findings introduce a novel therapeutic approach for radiation protection and treatment, with potential clinical applications.



Key Words: Radiation dermatitis; Reactive oxygen species; Inflammatory regulation; Curcumin; Tannic acid; Hydrogel patch

Acknowledgements: This research was supported by the National Natural Science Foundation of China (Grant No. 82273570); the "Pioneer" and "Leading Goose" R&D Program of Zhejiang (Grant No. 2024C03044); the Wenzhou Bureau of Science and Technology (NO. Y20240118).

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Mesenchymal Stem Cell-Derived Exosomes Enable Brain Delivery of Bioactive Phosphorous Dendrimers and Quercetin to Tackle Parkinson's Disease *via* Cooperative Modulation of Inflammatory Immune Microenvironment

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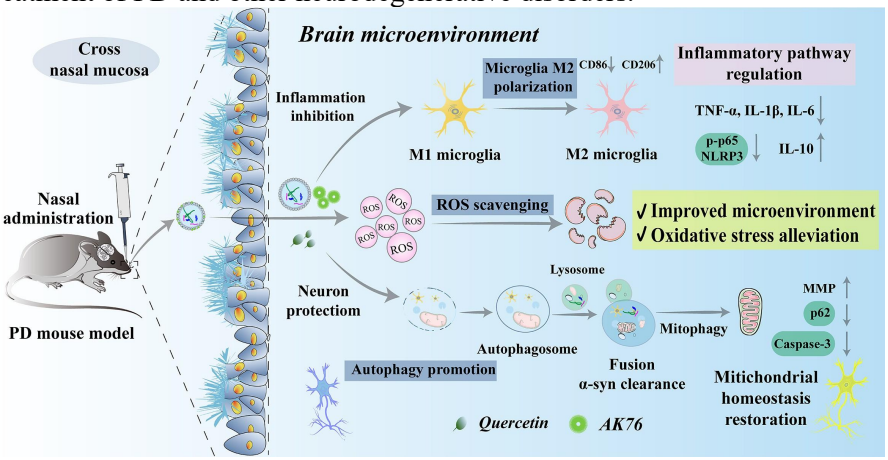
The intricate pathologic features of Parkinson's disease (PD) coupled with the obstacle posed by the blood-brain barrier (BBB) significantly limit the efficacy of most medications, leading to difficulties in PD treatments. Herein, we have developed a novel nanomedicine based on stem cell-derived exosomes co-loaded with hydroxyl-terminated phosphorus dendrimers (AK76) and quercetin (Que) for combined therapeutic intervention of PD. The engineered nanocomplexes (for short, QAE NPs) exhibit an optimal size of 269.7 nm, favorable drug release profile and desired cytocompatibility, enabling penetration of the nasal mucosa to accumulate in the brain without BBB crossing. The developed QAE NPs can scavenge reactive oxygen species, promote M2 microglial polarization, attenuate inflammation, and protect neurons by inducing autophagy and restoring mitochondrial homeostasis through the integrated anti-inflammatory and antioxidant properties of exosomes, Que and AK76, collectively leading to improved motor functions, coordination, and alleviation of depression-like symptoms of PD mice. The formulated QAE NPs combined with several therapeutic components are able to simultaneously modulate both microglia and neurons, offering a promising potential for the treatment of PD and other neurodegenerative disorders.



Scheme 1. Construction of QAE NPs for the combined treatment of PD *via* oxidative stress alleviation, microglia M2 polarization, autophagy promotion, and neuron protection.

Key Words: phosphorus dendrimers; exosomes; microglia M2 polarization; autophagy promotion; Parkinson's disease

Acknowledgements: This study was financially supported by the National Key R&D Program (2024YFE0108100), the National Natural Science Foundation of China (U23A2096, 52350710203, W2433053 and W2421104), the Science and Technology Commission of Shanghai Municipality (24490711000, 23520712500 and 20DZ2254900) and the China-Central and Eastern European Countries (CEEC) Joint Education Project (2023256).

Symposia 21

Neural Medical Engineering

3D bioprinted dynamic bioactive living construct enhances mechanotransduction-assisted rapid neural network self-organization for spinal cord injury repair

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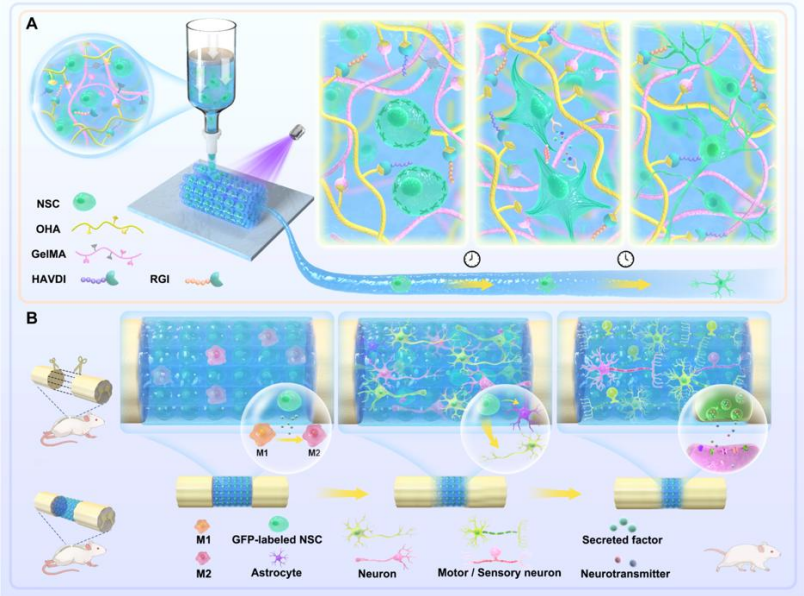
Biomimetic neural substitutes, constructed through the bottom-up assembly of cell-matrix modulus via 3D bioprinting, hold great promise for neural regeneration. However, achieving precise control over the fate of neural stem cells (NSCs) to ensure biological functionality remains challenging. Cell behaviors are closely linked to cellular dynamics and cell-matrix mechanotransduction within a 3D microenvironment. To address this, a dynamic bioactive bioink is designed to provide adaptable biomechanics and instructive biochemical cues, specifically tailored for the fate commitment of NSCs, through incorporating reversible Schiff-base bonds and bioactive motifs, N-cadherin-mimicking and BDNF-mimicking peptides. We demonstrate that the dynamic properties of 3D bioprinted living fibers alleviate the mechanical confinement on NSCs and significantly enhance their mechanosensing, spreading, migration, and matrix remodeling within the 3D matrix. Additionally, the inclusion of N-cadherin-mimicking and BDNF-mimicking peptides further enhances cells' ability to sense and respond to mechanical and neurotrophic cues provided by the surrounding matrix, which accelerates the self-organization of a functional neural network within the 3D bioprinted construct, leading to significant motor and sensory function recovery in a rat complete spinal cord injury model. This work underscores the critical role of precisely designing cell-instructive bioinks for the advanced functionality of 3D bioprinted living constructs in neural regeneration.



Key Words: 3D bioprinting, dynamic bioink, neural stem cells, biomechanical cues, biochemical cues, spinal cord injury

Acknowledgements: J. Yang., K. Kim. and Y. Liu. contributed equally to this study. The authors thank the financial support from the National Natural Science Foundation of China (Grant No. 32271414 and 82301560).

INTEGRATING HYDROGEL FOR SPINAL CORD INJURY REPAIR

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Introduction

Insufficient integration between implanted biomaterials and the native spinal cord is a recognized challenge in SCI repair, as it would cause inefficient growth of regenerating axons into grafts, ultimately leading to failure of neural regeneration.

Research design

A bioinspired hydrogel composed of hyaluronic acid-graft-dopamine (HADA) and a designer peptide HGF-$(RADA)_4$-DGDRGDS(HRR) was presented to enhance tissue integration following spinal cord injury (SCI).

Results and discussion

The HADA/HRR hydrogel manipulated the infiltration of $PDGFR\beta^+$ cells in a parallel pattern, transforming dense scars into an aligned fibrous substrate that guided axonal regrowth. Further incorporation of NT3 and curcumin promoted axonal regrowth and survival of interneurons at lesion borders, which served as relays for establishing heterogeneous axon connections in a target-specific manner. Notable improvements in motor, sensory, and bladder functions resulted in rats with complete spinal cord transection. The HADA/HRR + NT3/Cur hydrogel promoted V2a neuron accumulation in ventral spinal cord, facilitating the recovery of locomotor function. Meanwhile, the establishment of heterogeneous neural connections across the hemisected lesion of canines was documented in a target-specific manner via neuronal relays, significantly improving motor functions.

Conclusion

Biomaterials can inspire beneficial biological activities for SCI repair.

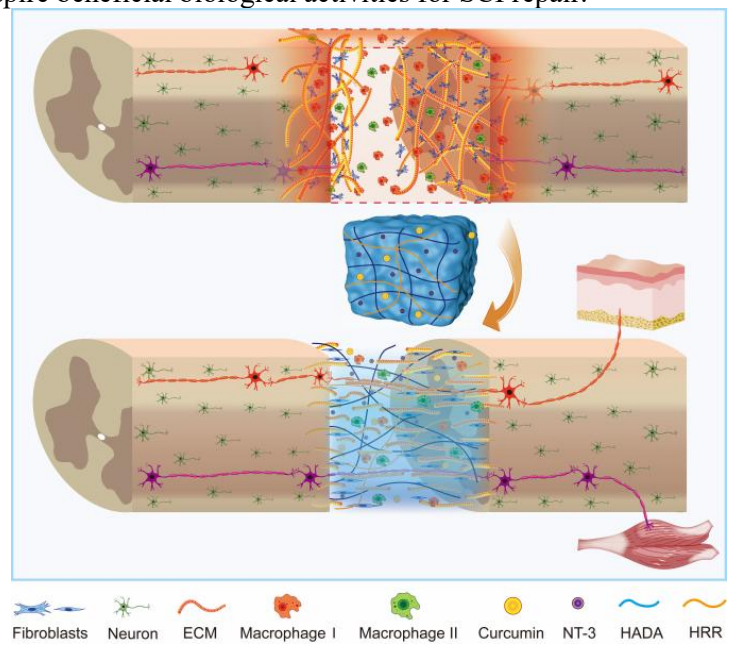

Figure. Integrating hydrogels manipulate ECM deposition for specific neural reconnections

Key Words: Spinal cord injury, bioinspired hydrogel, self-healing, ECM deposition

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Counteracting immunodepression by extracellular matrix hydrogel for traumatic brain injury repair

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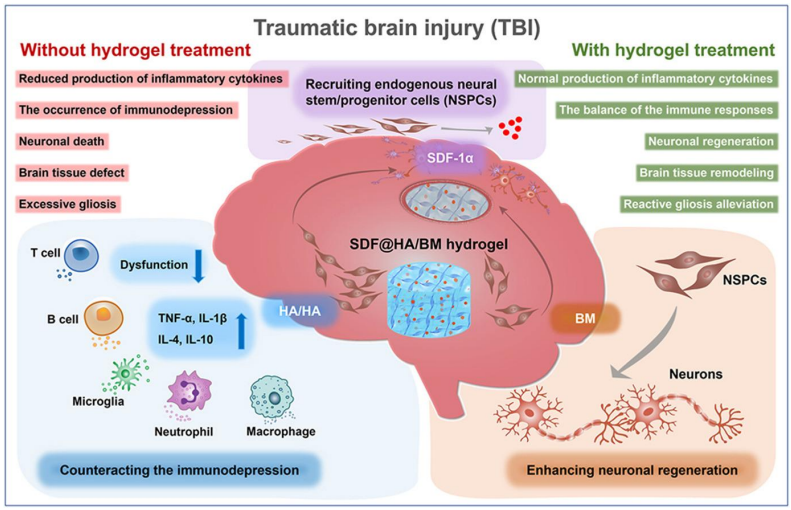
Abstract: Traumatic brain injury (TBI), an intractable disorder of the central nervous system (CNS), is a leading cause of long-term disability and mortality in humans worldwide. However, there is still no effective therapy for TBI, and an important reason for this is TBI-induced immunodepression, which renders TBI patients with low resistance to infections and aggravated brain damage. In this study, a multifunctional extracellular matrix hydrogel was constructed for the treatment of TBI in terms of both counteracting the immunodepression and enhancing neurogenesis. The stromal cell-derived factor-1α (SDF-1α)-loaded hyaluronic acid (HA)/decellularized brain extracellular matrix (BM) hydrogel (SDF@HA/BM) not only mimicked the composition and the biological cues of brain extracellular matrix, but also exhibited the injectability, self-healing, and mechanical properties close to those of brain tissue. The SDF@HA/BM hydrogel protected activated immune cells from dysfunction during the acute phase of TBI for normal levels of inflammatory cytokines, thereby creating a favorable immune microenvironment for subsequent neurogenesis. The SDF-1α and the BM synergistically promoted neurogenesis after TBI by recruiting endogenous neural stem/progenitor cells and inducing their differentiation into neurons. In vivo results demonstrated that the SDF@HA/BM hydrogel exhibited desirable therapeutic effects in severe TBI mice through facilitating brain tissue remodeling and neurological function recovery, including limb balance, autonomous locomotion, and spatial learning and memory abilities, and relieving depression and anxiety. Our work provides a novel strategy for TBI treatment in terms of restoring immune homeostasis and enhancing neurogenesis using advanced biomaterials.



Key Words: Central nervous system injury, Immunosuppression, Neuronal regeneration

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Peripheral Nerve Injury and Regenerative Microenvironment

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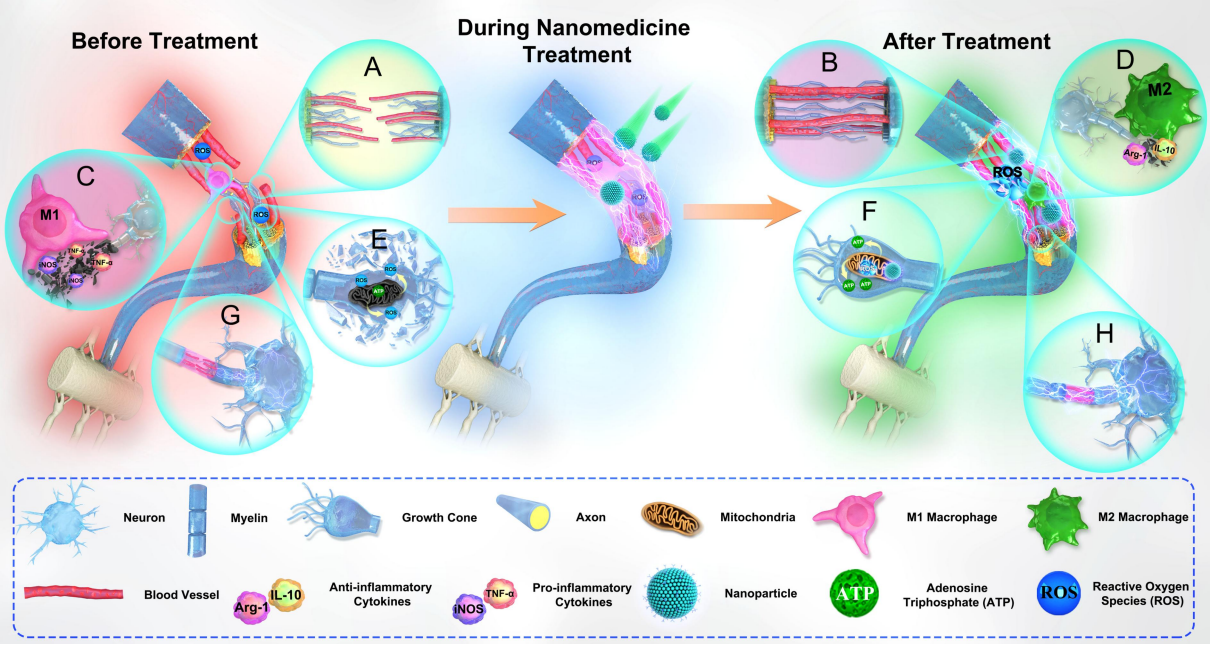
Neuronal microenvironment imbalance is associated with successive and irreversible pathophysiological changes and insufficient functional restoration after peripheral nerve injury. Conventional neural-supporting scaffolds result in unsatisfactory curative effects due to lack of biomimetic nanotechnology designs and biochemical or physicochemical modifications. Consequently, they fail in rational and facile remodeling of the imbalanced growth microenvironment, and cannot recover neural structure and function. In recent years, with the increasing knowledge in neuronal injury-associated microenvironment, a number of novel strategies are applied in enhancing the biochemical and physicochemical natures of biomimetic nanomaterial-based scaffolds for nerve tissue engineering. These scaffolds can trigger growth factor secretion and aggregation through surface modification, regulate ATP synthesis and hydrolysis, switch between oxidation and reduction states, and activate ion channels and stimulate electrical signals under certain biophysical cues. Consequently, they can determine neuronal cell fate by modulating their viability, development and cell cycles during the regeneration process. In this work, we summarize the studies on the biomimetic scaffold design of functional materials, their basic topological, biochemical and physical properties, and nanotechnology-based restoration of a balanced nutritional microenvironment regarding four key neural regeneration factors, including immune response, intraneural vascularization, bioenergetic metabolism and bioelectrical conduction in order to provide ideas and inspiration for the nanomedicine-based neuronal regeneration therapy.



Key Wards: (peripheral nerve injury, microenvironment, biomaterials, tissue regeneration)

Acknowledgements: (None)

Symposia 22

New Techniques and Methods for Tissue Repair

Developing an enzyme-free adipose stem cell extraction method from buccal fat pad for oral-maxillofacial bone regeneration

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Oral-maxillofacial bone defects are challenging to restore due to complex anatomy of the oral region and lack of vascularization in bone graft treatments. Adipose-derived mesenchymal stem cells (ADMSCs) are becoming popular for regenerative medicine due to their less invasive harvest and high cell yield. ADMSCs can be extracted from the buccal fat pad, a fatty tissue located in the cheek, but traditional methods to isolate ADMSCs involve collagenase, face regulatory hurdles. The objective of this study is to develop and evaluate an enzyme-free method to extract ADMSCs from buccal fat pad for oral-maxillofacial bone regeneration. In this study, we isolated adipose tissue from the abdomen region and buccal fat pad in adult pigs, which have similarity physiology and adipose tissue composition as human. The harvested adipose tissue was divided into 0.1g portions and subjected to the following conditions: (1) enzymatic digestion with collagenase, papain and bromelain, (2) mechanical disruption using a proprietary tissue grinder, with 3 different settings: soft, medium or harsh. After enzymatic digestion or mechanical disruption, the mixture was separated with a sieve. The cell count and cell vitality in the filtrate and residue were then evaluated and compared.

Our results showed that while enzymatic digestion with collagenase is effective, mechanical disruption using tissue grinder creates a toothpaste-like extract suitable for direct use in tissue engineering applications. We observed the presence of fibrous debris in the residue and we are currently investigating the effects of fibrous debris in bone regeneration. We will continue to optimize the protocol to extract ADMSCs from buccal fat pad using the tissue grinder. The successful development of an enzyme-free extraction method would allow ADMSCs to be easily and rapidly seeded into bone scaffolds and implanted into oral-maxillofacial defect sites, allowing the whole process from tissue harvest to scaffold implantation to be done within one surgery session, thus saving time and costs for patients and the clinic.

Key Words: Bone regeneration, adipose stem cells, buccal fat pad, enzyme-free

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Figure 1: Schematic diagram of study with surgical photos of the adipose tissue extraction

AI-Driven Design of Nerve Conduits for Advanced Mechanical-Electrical Microenvironment Control in Nerve Regeneration

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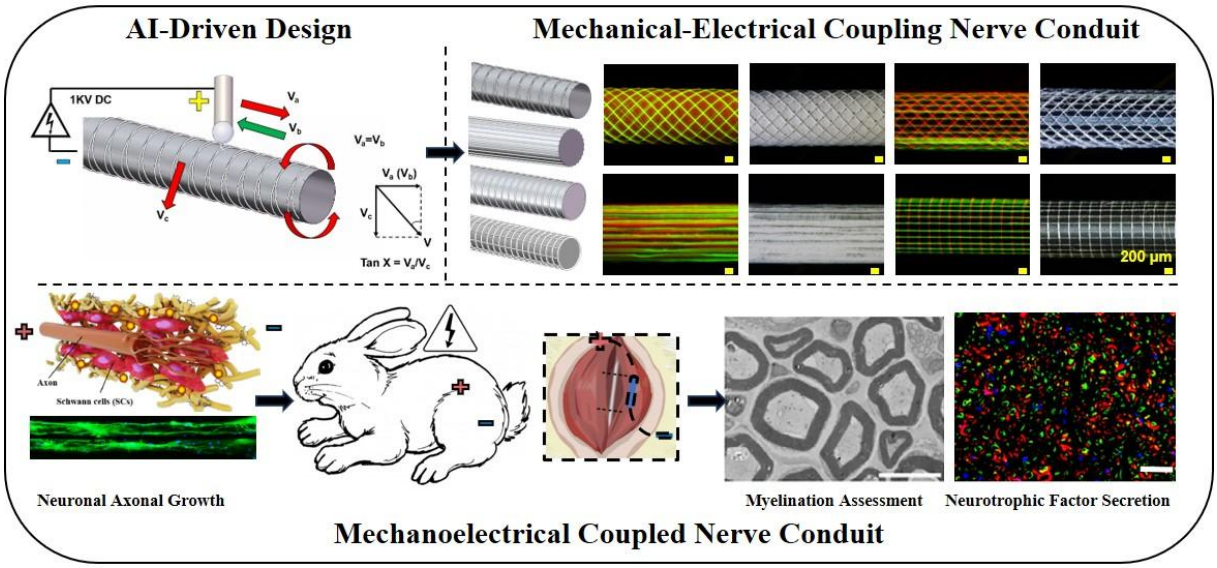
Long-distance peripheral nerve regeneration (>30 mm) presents a major challenge in neural tissue engineering. Nerve conduits, as biomaterials, aid regeneration by reconstructing the cellular microenvironment. Studies show that mechanical and electrical factors jointly influence axonal growth, glial myelination, and neurotrophic factor secretion. While electrical stimulation has improved axonal regeneration in previous studies, controlling both mechanical and electrical properties in conduit fabrication remains difficult, obscuring the mechanisms behind their coupled effects. To address this, our research integrates AI and advanced 3D printing to modularly fabricate composite nerve conduits, creating a platform to precisely control the mechanical-electrical microenvironment. By adjusting conduit topology, stiffness, conductivity, and electrical stimulation, we achieve fine-tuned spatiotemporal modulation of the microenvironment. The regenerative effects of these conduits are evaluated in large-animal models. This work explores the multiscale mechanical and electrical properties of biomaterials, offering novel insights for the biomimetic design and clinical application of nerve conduits.



Key Words: Nerve Conduits; Mechanical-Electrical Coupling; Peripheral Nerve Regeneration; 3D Printing.

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Biosynthesis of Lysosomally Escaped Apoptotic Bodies Inhibits Inflammasome Synthesis in Macrophages

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Abstract:

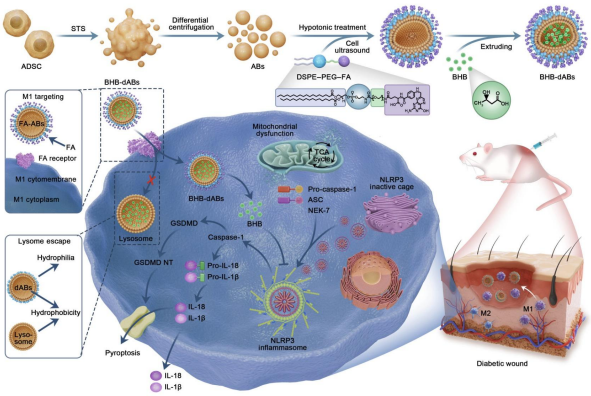
Background: Hyperglycemia and bacterial colonization in diabetic wounds abnormally activate NLRP3 in macrophages, leading to excessive inflammation and impaired healing. Targeted NLRP3 suppression holds promise but faces challenges like off-target effects and lysosomal degradation.

Methods: Engineered apoptotic bodies (BHB-dABs) from adipose stem cells loaded with BHB target M1 macrophages via folate receptor recognition and promote lysosomal escape through DSPE-PEG modification, potentially enhancing NLRP3 inhibition in diabetic wound treatment.

Findings: *In vitro* studies demonstrated that BHB-dABs are biocompatible, selectively target M1 macrophages, and release BHB within the inflammatory microenvironment via folic acid receptor (FAR). These nanovesicles exhibit lysosomal escape, anti-inflammatory effects, mitochondrial protection, and pro-angiogenic activity. *In vivo*, BHB-dABs promote inflammation resolution and angiogenesis in diabetic wounds, thereby accelerating healing.

Discussion: These functionalized apoptotic bodies efficiently deliver NLRP3 inflammasome inhibitors using a dual strategy of targeting macrophages and promoting lysosomal escape.

Conclusion: This approach represents a novel therapeutic strategy for effectively treating chronic diabetic wounds.



Key Words: Apoptotic Bodies, NLRP3 Inflammasome, Lysosome escape, Diabetic wounds, Macrophage targeting

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Lubricated injectable electroactive short fibers facilitate cartilage repair through piezoelectric conversion

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Objective: The degradation of extracellular matrix (ECM) and joint wear caused by the interruption of endogenous electric fields (EF) are the core pathological bases of osteoarthritis (OA). How to restore the endogenous EF while enhancing the lubrication performance between articular cartilages and achieving a balance in ECM catabolism is the key to reversing OA and promoting cartilage repair.

Methods: In this study, "PLA/Gel@β-Gly/GO/PMPC" lubricating electroactive short fibers were constructed using microgel electrospinning technology and a one-step surface dopamine grafting technique. By using an "ultrasonic piezoelectric transducer" to generate electrical signals, the synthesis of ECM was promoted, the endogenous EF was restored, and the hyaluronic lubrication layer was repaired, achieving the dual effects of stabilizing the endogenous EF and realizing the regeneration and optimization of articular cartilage, thereby reversing the adverse cycle of OA.

Results: (1) Electroactive effect: Under ultrasonic stimulation of 1 W, 650 kHz, and 50% duty cycle, the electroactive short fibers generated a 1.31 V electrical signal, which significantly upregulated the expression of Sirt1 in OA chondrocytes, improved mitochondrial function, increased ATP production to 23.074 ± 1.87 pmol/min, promoted ECM synthesis, and restored the endogenous EF. (2) Lubrication performance: The supplementation of different proportions of lubricating molecules (1:1, 1:4, 1:8) reduced the coefficient of friction (COF) between articular cartilages from 0.725 and 0.693 to approximately 0.235, enhanced the lubrication performance between articular cartilages, inhibited ECM degradation, and stabilized the endogenous EF.

Conclusion: This study is the first to integrate piezoelectric effects and boundary lubrication mechanisms into a composite material system. The electroactive components activate the Sirt1/mitochondrial pathway by restoring EF homeostasis, promoting ECM synthesis; PMPC lubricating molecules inhibit ECM degradation induced by mechanical wear through the reconstruction of the hyaluronic lubrication layer. This innovative composite electrospun material breaks the vicious cycle between endogenous EF and ECM degradation and joint wear, showing great potential in promoting OA cartilage repair.

Keywords: injectable, electroactive, short fiber, lubrication disturbance, mitochondrial damage, vicious cycle

Ultrasound-Responsive Electroactive Hydrogel Modulates Macrophage Electrophilic Stress to Disrupt Inflammatory Vicious Cycle and Promote Tendon-Bone Healing

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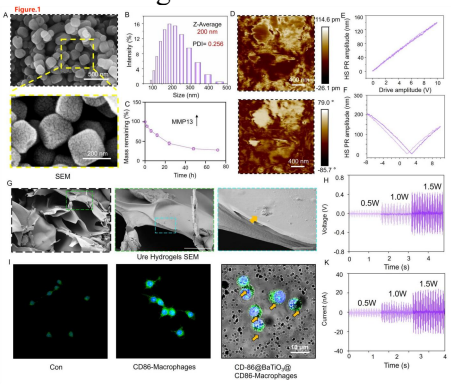
Abstract: The persistent aberrant activation of pro-inflammatory macrophages triggered by the injury-induced inflammatory microenvironment is a pivotal contributor to tendon-bone interface healing impairment. Enhancing macrophage resilience to counteract the inflammatory microenvironment has emerged as a critical strategy for improving tendon-bone healing. Electrical stimulation, with its dual anti-inflammatory and pro-regenerative effects, represents an ideal therapeutic approach for modulating inflammatory responses at the tendon-bone interface. However, achieving precise electrical regulation of macrophages remains challenging. To address this, we developed a novel ultrasound-responsive electroactive hydrogel (Ure Hydrogels), whose matrix is degraded by MMP13 specifically expressed in the inflammatory microenvironment, thereby releasing CD86-BaTiO3 nanoparticles. Through external ultrasound-triggered sonoelectrical conversion, this system enables precise targeting of CD86+ pro-inflammatory macrophages. We first validated the material characterization, biocompatibility, and targeting specificity of Ure Hydrogels. In vitro experiments demonstrated that the hydrogel effectively blocks inflammatory cascades in LPS- and DAMPs-induced pro-inflammatory polarization models of macrophages. Animal studies confirmed that Ure Hydrogels significantly alleviated local inflammation at the tendon-bone interface and comprehensively improved healing phenotypes. Mechanistic studies indicate that alterations in electron transfer between nucleophilic and electrophilic molecules, which modulate the electrophilic stress response in macrophages, may constitute a critical molecular event underlying the enhancement of macrophage resilience. In conclusion, the developed Ure Hydrogels achieve ultrasound-triggered sonoelectrical conversion to target pro-inflammatory macrophages, enhance macrophage resilience via regulation of electrophilic stress, thereby disrupting the inflammatory vicious cycle and promoting functional tendon-bone healing.



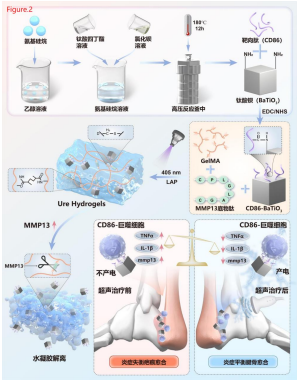


Figure.1: Partial characterization of Ure Hydrogels; **Figure.2**: Ure Hydrogels regulate the balance of inflammation to promote tendon-bone healing.

Key Words: Ure Hydrogels, macrophage resilience, electrophilic stress, tendon-bone healing

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Short Fiber Nasal Drops for Treating Brain Neurological Disorders

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Introduction

Nasal administration as a non-invasive route for drug delivery to the brain has been a focal point in the field of neuroscience [1]. However, multiple barriers associated with the nasal-to-brain drug delivery pathway, such as nasal formulation toxicity to cilia, rapid clearance of nasal mucosal cilia, and enzymatic degradation, present significant challenges for targeted nasal drug delivery. Thus, it is important to develop a novel noninvasive method for cerebral drug delivery.

Research design

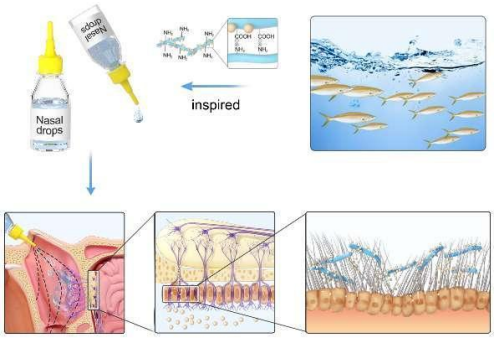
Inspired by swimming fish and the microstructure of the nasal cavity, short-swimming fibrous nasal drops with the ability to transport drugs along the nasal mucosa were innovatively constructed by guiding electrospun fibers into the swimming short fibrous nasal drops *via* electrospinning, homogenization, and subsequent multifunctional modifications to achieve precise intraventricular administration by targeting the nasal mucosa and controlling drug release along with the swing of the nasal cilia.

Results and discussion

The unique specific surface area and positive surface charge of drug-loaded short fibrous nasal drops contribute to adequate adhesion to the nasal mucosa, prolonged residence time, and avoidance of rapid nasal mucociliary clearance. After being triggered by the nasal cilia wiggle, the loaded drug was rapidly released from the fibers and arrived at the brain *via* the olfactory and trigeminal nerve pathways.The *in vivo* and *in vitro* experiments proved that the drug-loaded short fiber nasal drops had good biocompatibility and could effectively target the delivery of drugs in the nasal mucosa to the brain, weaken the inflammatory response in microglia through the release of LRRK2 inhibitors, improve synaptic plasticity, and alleviate cognitive impairment in SAE.

Conclusion

The electrospun short fiber nasal drops developed in this study can deliver drugs to the brain by targeting the nasal mucosa, and effectively improve the learning and cognitive ability of sepsis mice by releasing LRRK2 inhibitors. In conclusion, this study provides a new material carrier and research idea for the treatment of brain diseases.



Keywords: Electrospun short fibers, Nasal mucosa, Intraventricular administration, Brain diseases

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Bionic scaffolds/microspheres from Microfluidics for Bone Regeneration

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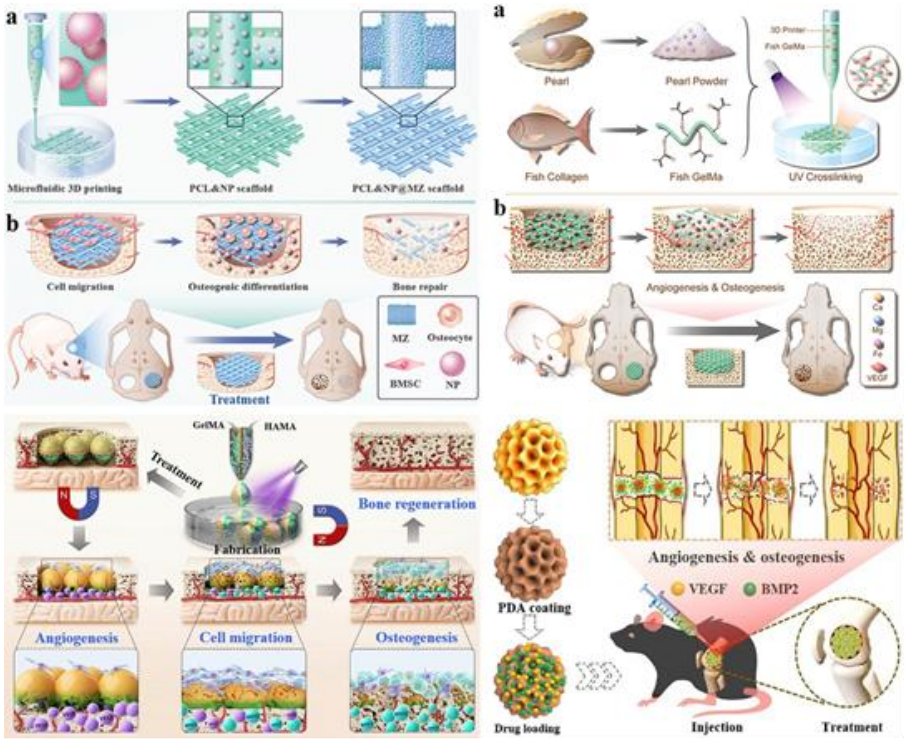
Introduction: Large bone defects caused by trauma, disease, or congenital conditions remain a major clinical challenge, as they often exceed the body's natural regenerative capacity. Current therapies face limitations in efficacy, complexity, and cost. Microfluidic technology offers unique advantages for tissue engineering by enabling precise fabrication of biomaterials with controlled microstructures, compositions, and bioinspired functionalities that mimic the native bone environment. This study focuses on developing biomimetic microspheres and scaffolds using microfluidic approaches to accelerate bone regeneration.

Research Design: Our strategy combines microfluidic 3D printing and electrospray techniques to engineer bone regenerative platforms. Key objectives include: (1) fabricating scaffolds with tunable porosity and bioactive components (e.g., minerals, pearl powder) to replicate bone composition via microfluidic 3D printing; (2) designing functional microparticles (e.g., Janus microspheres, dual-adhesive carriers) for sequential growth factor release or enhanced tissue adhesion using microfluidic assembly; and (3) developing microcapsules via microfluidic droplet generation to encapsulate and deliver stem cells. Materials such as biocompatible polymers, hydrogels, inorganic biomaterials, and stem cells were integrated to achieve multifunctional therapeutic systems.

Main Results and Discussion: Through microfluidic 3D printing, we successfully constructed sophisticated biomimetic scaffolds. Notably, we developed mineralized organic-inorganic hybrid scaffolds with highly ordered structures mimicking natural bone, which demonstrated enhanced osteogenic differentiation and vascularization potential *in vitro* and *in vivo* [1]. Pearl powder-incorporated hybrid scaffolds, also fabricated via microfluidic 3D printing, leveraged natural bioactive components to promote bone regeneration [2]. Beyond scaffolds, microfluidic engineering yielded functional microparticles. Bio-inspired Janus microcarriers were designed to achieve sequential release of distinct bioactive agents, mimicking the temporal dynamics of natural bone healing [3]. Furthermore, microfluidic electrospray enabled the production of dual-adhesive particles designed to improve localization and integration within the defect site [4]. We also developed biomass-derived microcapsules via microfluidics for effective mesenchymal stem cell encapsulation, maintaining high cell viability and facilitating targeted cell delivery for bone repair [5]. These engineered systems consistently showed improved performance compared to simpler controls in relevant assays, highlighting the benefits of precise microfluidic control over material structure and function for directing bone tissue regeneration.

Conclusion: Our research demonstrates the significant capability of microfluidic technologies to engineer a versatile toolbox of advanced, biomimetic microsystems tailored for bone regeneration. By enabling precise control over architecture, composition, and functional properties (such as biomimicry, controlled release, enhanced adhesion, and cell delivery), microfluidics allows for the creation of sophisticated platforms that effectively interact with biological systems to promote bone healing. These microfluidic-derived scaffolds, microcarriers, and microcapsules hold considerable promise as next-generation therapeutic strategies for addressing challenging bone defects.



Key Words: Microfluidics, Microspheres, Bone Regeneration, Drug Delivery, Stem Cells.

Acknowledgements:

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Secretory Fluid-Aggregated Janus Electrospun Short Fiber Scaffold for Wound Healing

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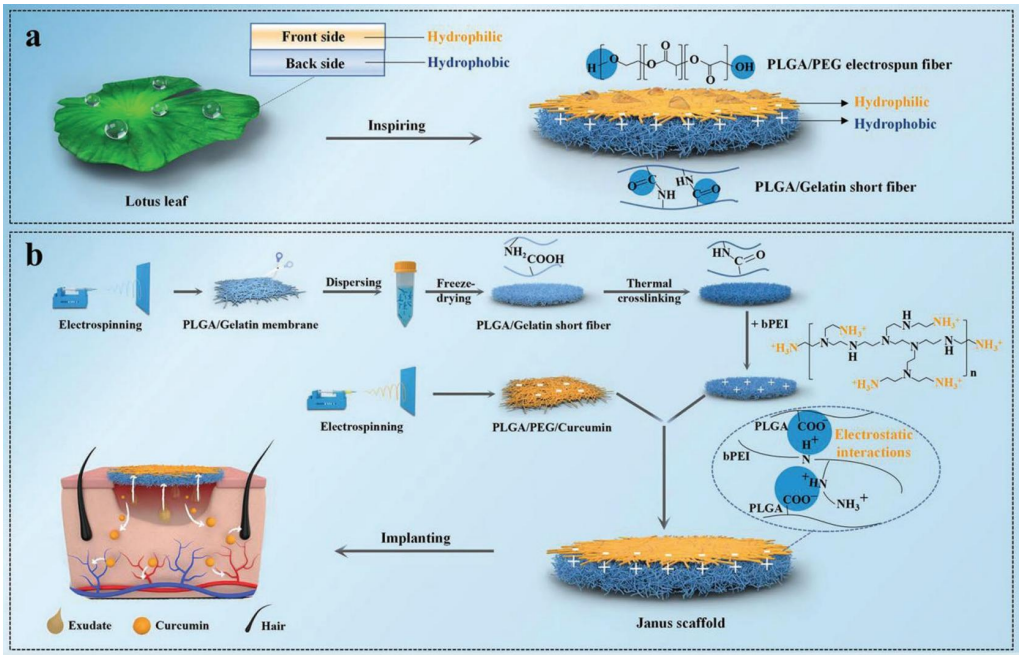
Exudate management is critical to improve chronic wound healing. Herein, a Janus electrospun short fiber scaffold is fabricated via electrospinning technologies and short fiber modeling. This scaffold is composed of hydrophilic 2D curcumin-loaded electrospun fiber and hydrophobic 3D short fiber *via* layer-by layer assembly and electrostatic interactions which can aggregate the wound exudate by pumping from the hydrophobic layer to the hydrophilic via multiple contact points between hydrophilic and hydrophobic fibers, and simultane ously trigger the cascade release of curcumin in the upper 2D electrospun fiber. The 3D short fiber with high porosity and hydrophobicity can quickly aggregate exudate within 30 s after compounding with hydrophilic 2D electrospun fiber. *In vitro* experiments show that Janus electrospun short fiber has good biocompatibility, and the cascade release of curcumin can significantly promote the proliferation and migration of fibroblasts. *In vivo* experiments show that it can trigger cascade release of curcumin by aggre gating wound exudate, so as to accelerate wound healing process and promote collagen deposition and vascularization. Hence, this unique biometric Janus scaffold provides an alternative for chronic wound healing.



Key Words: Janus structures; fluid-aggregated scaffolds; short fibers; wound exudates

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Self-Powered Medical Devices

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Electrical activity is fundamental to human biological functions. By regulating electrical activity, we can alter the excitation and inhibition states of cells, tissues, and organs, thereby achieving disease treatment. Nanogenerators are a new type of energy conversion device that can convert low-frequency mechanical energy into electrical energy. Due to the diverse and flexible structures, a wide range of selectable materials, and high output voltage, nanogenerators offer novel approaches for developing self-powered medical devices. Our research has developed several innovative systems based on this technology: 1. Self-powered cardiac pacemakers powered by heartbeat-derived energy, which can operate long-term, and for the first time, conducted large animal experiments to enhance heart rates and treat arrhythmias. 2. Fully biodegradable self-powered electrical stimulation devices which directionally guide neural growth, enhance cardiomyocyte electrical coupling, promote osteogenesis, and accelerate wound healing before complete biosorption post-therapy. 3. Closed-loop self-powered LL-VNS system that can monitor the patient's pulse wave status in real time and conduct stimulation impulses automatically during the development of atrial fibrillation with minimizing neurological side effects. 4. Minimally invasive implantable biosensors with exceptional biocompatibility for continuous cardiovascular monitoring. These studies focus on self-powered electronic medical devices and electrical stimulation therapy, holding significant potential for transformation into clinically usable electronic medical devices and sensors.

Key Words: self-powered, medical devices, biosensors, electrical stimulation devices, nanogenerators

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Symposia 23

Scaffold Design and Fabrication

Antifouling and high permeability hydrogel devices for long-term immunoisolation of islet transplants in type 1 diabetes

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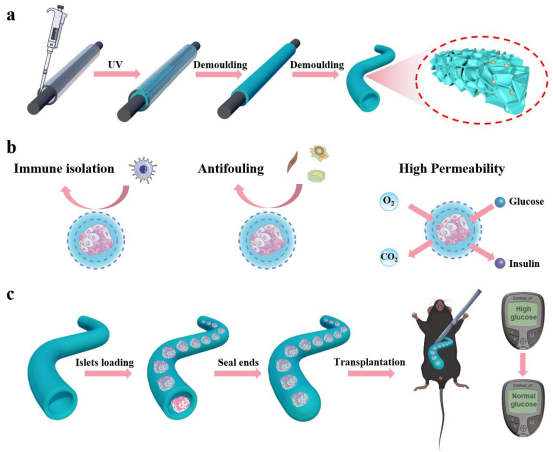
Introduction: Type 1 diabetes (T1D) is an autoimmune disorder mediated by T cells, characterized by the specific destruction of pancreatic β-cells, resulting in absolute insulin deficiency [1]. While pancreatic islet transplantation represents a promising therapeutic approach, challenges such as donor shortages and the need for immunosuppressive therapies persist [2].

Research design: We developed a long-term stable, highly biocompatible, highly permeable, and immunoisolative flexible hydrogel for islet encapsulation. This study presents a novel, flexible hydrogel encapsulation material, incorporating functional monomers such as NAGA, CBAA, and SiGMA, which are polymerized through a free-radical polymerization reaction.

Main results: The resulting hydrogel device demonstrates excellent biocompatibility, antifibrotic properties, and high oxygen permeability, while effectively mitigating immune rejection and supporting long-term islet cell survival and function. Experimental results show that hydrogel-encapsulated islet cells enable diabetic mice to restore normal blood glucose levels, with islet cell survival maintained for up to 180 days.

Discussion: The flexible hydrogel device designed in this study successfully achieved immunoisolation of islet cells and enhanced cell viability by incorporating multiple functional monomers. In Vivo, the device demonstrated excellent oxygen permeability and anti-fibrotic properties, effectively preventing external immune responses while providing essential nutrients and oxygen to the islet cells.

Conclusion: This flexible hydrogel device presents a promising solution for type 1 diabetes cell replacement therapy, with broad prospects for future clinical applications.



Key Words: Type 1 diabetes, islet encapsulation, hydrogel device, immunoisolation

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In Situ Autonomous Pore-forming Polyphosphate Coacervate-based injectable bone substitutes

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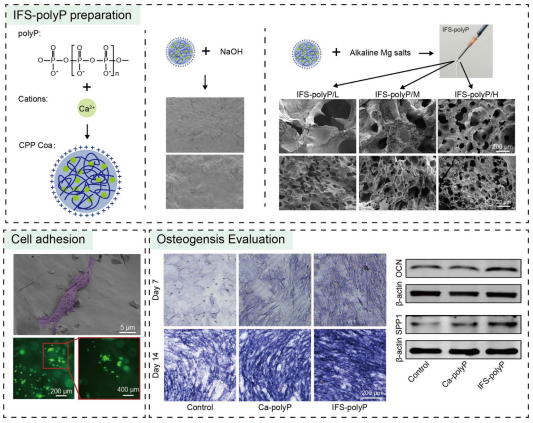
Introduction: Porous structures are pivotal in bone regeneration by facilitating nutrient exchange, enabling bone tissue and vascular ingrowth. While porogen-assisted methods have achieved controlled porous scaffolds preparation, their dependence on exogenous pore forming agents carries the risk of residual cytotoxicity. Current fabrication methods, such as gas foaming and phase separation, still not enable in situ autonomous pore formation without porogens additives[1]. This critical limitation has prompted us to develop porogen-free, in situ autonomous pore-forming bone substitutes, avoiding the cytotoxicity of additives and potentially enhancing bone integration potential.

Research design: Take advantage of calcium polyphosphate coacervates (CPP coa) formed via liquid-liquid phase separation between endogenous polyphosphate chains and Ca^{2+} ions[2], we prepared a porogen-free, injectable, pore-forming, self-setting polyphosphate-based composites (IFS-polyP). The design capitalizes on CPP coa's dual functionality: (1) pH-responsive deprotonation enabling self-setting, and (2) spontaneous pore generation through controlled aqueous phase entrapment.

Main results and discussion: IFS-polyP demonstrated porogen-free in situ autonomous pore-forming through a hypothesized mechanism: (1) viscous CPP coa matrices inhibited water migration during cement setting, and (2) faster superficial setting further blocked water diffusion, thus generated encapsulated "aqueous microdomains" that evolved into interconnected macropores. *In vitro* experiments results showed that IFS-polyP has excellent biocompatibility, allowing cells ingrowth and promoting cell osteogenic differentiation.

Conclusion: This work establishes a novel porogen-free platform for injectable bone substitutes with in situ autonomous pore-forming capability. Further study on the coacervate-based pore formation mechanism may establish a novel paradigm for pore construction of biomaterials and open new avenues for clinical translational study of injectable bone implants.



Key Words: in situ autonomous pore-forming, polyphosphate, coacervate, bone repair

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Tissue-scaffold-mimicking electronics for seamless integration of electronics with living tissues

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Bioelectronics represents rapidly developing analytical tools with electrophysiological studies in fundamental biological sciences, biotechnology, and medicine. Despite these potentials, seamless integration of electronics with living tissues has been difficult due to intrinsic mismatches, including size and mechanical properties, between the elements of the electronic and living systems. To bridge the gap, we have developed the new concept of tissue-scaffold-mimicking electronics that resembles the structural, mechanical and topological properties similar to those of artificial tissue-scaffold materials; therefore fusing of the two can be seamless. This talk will first introduce our recent progresses on the development of unfoldable tissue-scaffold-mimicking electronics which can be delivered into animals' central nerve system in a precise and minimally-invasive way. It will showcase the seamless integration of electronics in living animals with suppressed acute implantation damage and chronic immune response simultaneously. This talk will later discuss the fusing of tissue-scaffold-mimicking electronics with synthetic tissues in vitro where longitudinal electrophysiology across the period of tissue engineering can be achieved, and will conclude on potential exploration on multi-modality synergy of electronic method with other cutting-edge biosensing technologies.

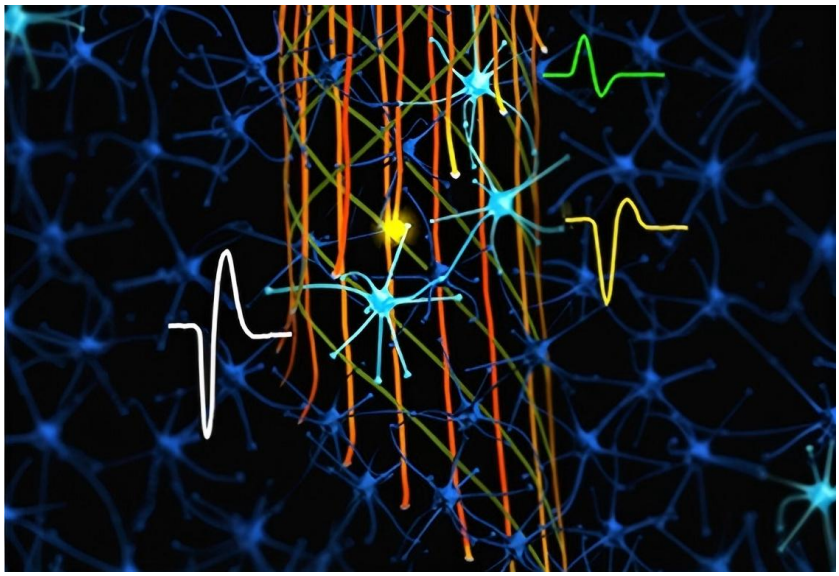

Fig.1 Seamless Integration of Electronics with Living Animals

Key Words: Flexible electrodes, Brain-machine Interfaces, Tissue engineering, Biosensors

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nCaP-Reinforced PCL Composites for Bone Repair Application

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Polycaprolactone (PCL) based composites have emerged as promising candidates for complex musculoskeletal regeneration, yet their adaptation to multi-tissue interfaces—such as tendon-to-bone junctions and periosteal defects—remains underexplored. This study presents a dual-functional design of nano-calcium phosphate (nCaP)/PCL composites tailored for both tendon-to-bone repair and periosteum-mimicking regeneration. For tendon-to-bone application, a gradient-structured scaffold was fabricated by integrating nCaP into a PCL matrix, creating a mechanical transition zone that mimics the natural tendon–bone interface. Simultaneously, a flexible yet osteoinductive membrane for periosteal repair was developed by blending nCaP with PCL, achieving a balance of elasticity and bioactivity. This dual-strategy approaches addresses the limitations of conventional single-phase biomaterials and highlights the versatility of nCaP/PCL composites in multi-tissue regenerative applications.

Keywords: polycaprolactone, nano-calcium phosphate, tendon-to-bone interface, periosteum, composite biomaterials

Symposia 24

Self-adaptive biomaterials for Tissue Repair and Regeneration

Immunomodulating polymers for tissue repair and regeneration

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The degree of tissue injuries such as scarring or organ dysfunction primarily determine the outcome and speed of healing process. Different types of biomaterials are implanted either alone or by combined with other bioactive factors, which will interact with the immune systems to achieve different results. Several types of polymers and nanomaterials including polyurethane elastomers and hydrogels responding to reactive oxygen species (ROS) and MMP have been synthesized and fully characterized in terms of ROS or MMP-responsiveness, mechanical properties, degradation and ROS elimination in our lab. By integrating with other functional molecules such as methylprednisolone (MP), dexamethasone, dimethyl itaconate (DMI), and catalase etc., therapeutic materials systems such as nanofibrous patches, and injectable hydrogels, microgels and nanoparticles were designed and prepared for the treatment of myocardial infarction, osteoarthritis (OA) and lung inflammation etc. *in vivo*. These materials systems could effectively alleviate the inflammation microenvironment of tissues, and thereby could better restore the normal tissue microenvironment and achieve better tissue repair and regeneration. For example, they significantly reduced the ROS level in articular cavity and alleviate destruction of oxidative stress, and thus promoted significantly the therapeutic outcomes of OA with a best score close to the normal cartilage.

Keywords: Self-adaptive biomaterials; immunomodulating polymers; hydrogels; inflammation; tissue repair

Acknowledgements: This study is financially supported by the Joint Fund of National Natural Science Foundation of China (U22A20155), the National key research and development program of China (2023YFE0108700), and the State Key Laboratory of Transvascular Implantation Devices (012024004).

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Engineered Polysaccharide Hydrogel Orchestrates Oxidative Stress Alleviation, Immune Homeostasis, and Angiogenesis to Accelerate Wound Regeneration

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Wound repair involves a complex process that includes angiogenesis, immunomodulation and collagen deposition[1]. Polysaccharide hydrogels can provide suitable moisture to wounds, promote tissue regeneration, and can exhibit specific properties depending on the type of wound[2]. We developed a novel polysaccharide hydrogel (QK/KgXd^{gel}) that combines konjac glucomannan (KGM) modified with gallic acid (GA) and dopamine (DA)-conjugated xanthan gum (XG), which is then integrated with the vascular endothelial growth factor-derived peptide QK (KLTWQELYQLKYKKI). QK/KgXd^{gel} was characterized by UV and IR. Subsequently, the tube-forming ability of QK/KgXd^{gel} on HUVECs cells, polarization modulation of macrophages, and scavenging of ROS such as DPPH and hydrogen peroxide were explored in vitro. Finally, its effect on wound healing was assessed in a mouse model of total skin defect wounds. The results showed that QK/KgXd^{gel}-cultured macrophages had an elongation rate of 3.07±0.02, which was more than twice as high as that of the control group, showing an elongated shape and improved spreading morphology.QK/KgXd^{gel} reduced DPPH by 54%, and the fluorescence intensity of intracellular ROS levels, measured by the standard DCFH-DA assay, was almost the same as that in the QK/KgXd^{gel} group as the negative control group. In addition, QK/KgXd^{gel}-cultured HUVECs cells formed connected and compact tubes, showing denser tube intensity than the control group. On the third postoperative day, the wound area in the QK/KgXd^{gel} group (42.9% ± 0.7%) was significantly smaller than that in the control group (68.2% ± 0.6%). Compared with the control group, QK/KgXd^{gel} showed good pro-angiogenic, antioxidant and M2 macrophage polarization modulation properties, and demonstrated multifunctionality in synergistically promoting cutaneous wound healing, which makes it a highly promising wound healing agent.

Figure 1. Synthesis of KgXd^{gel}.

Key Words: Polysaccharide hydrogel, Wound healing, Oxidative stress mitigation, Angiogenesis stimulation, Immune regulation

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Selective and Responsive Antimicrobial Biomaterials for Combating Drug-resistant Bacterial Infections

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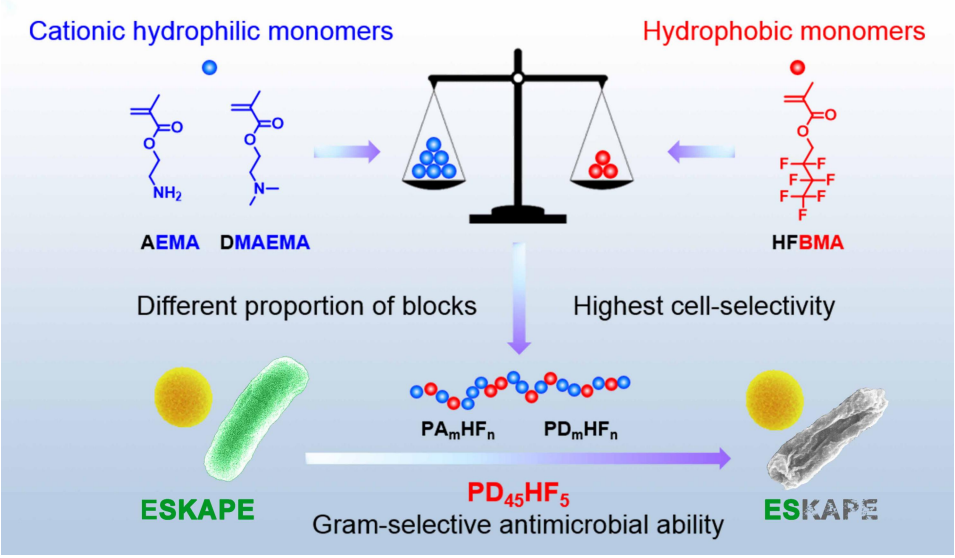
Bacterial resistance caused by the overuse of antibiotics and the shelter of biofilms has evolved into a global health crisis. In the past ten years, our group developed series of antimicrobial peptides/polymers, nanomaterials and wearable devices to fight against drug-resistant bacteria and biofilm-associated infections. Cationic peptides/polymers that act their bactericidal efficacy by disrupting bacterial cell walls have been synthesized, and applied as disinfectants, surface coating of biomedical devices, wound dressings, etc. We also developed several nanomaterials for high efficient eradication of bacterial biofilm based on photothermal/photodynamic/gas therapies. Selective antimicrobial materials have been designed by metallic labeling and molecular recognition. Moreover, wearable and implantable therapeutic devices were fabricated using flexible substrate materials loaded with our antimicrobial molecules or integrated with optoelectronics. These advanced antimicrobial materials and devices exhibited excellent efficacy towards drug-resistant bacteria, and could serve as alternatives of antibiotics in the future.



Key Words: antimicrobial polymers, wound dressing, photothermal, photodynamic, flexible devices

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Natural Macromolecule-Based Multifunctional Antibacterial Coatings

Shun Duan and Fu-Jian Xu

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This paper explores the "multifunctional surface modification of implantable medical devices" and introduces a convenient and versatile volatile film-forming method. The method involves designing a solution with film-forming, cross-linking, and antibacterial components, forming a coating by evaporating water from the solution. By optimizing these components, coatings were applied to various devices to meet practical needs. Key findings include:

(1) The study proposed a simple volatile film-forming method for constructing antibacterial and antifouling coatings. Using aldehyde-modified sodium alginate as a cross-linking component, gentamicin was loaded via a pH-sensitive Schiff base for responsive release. This method improved coating uniformity and thickness, maintaining an antibacterial effect after 7 days and effectively killing bacteria over five cycles.

(2) The Ti-GOG3 antibacterial bone plate was developed for orthopedic implants. With gelatin as the film-forming component, aldehyde-modified sodium alginate as the cross-linking component, and gentamicin as the antibacterial agent, Ti-GOG3 adaptively releases GS in response to infection, preventing inflammation in a rabbit tibia fracture model and promoting bone healing.[1]

(3) For urinary catheters, aldehyde-modified xanthan gum was used to create an antibacterial and antifouling coating (SR-GXG2) on silicone rubber. The method proved versatile across different substrates. SR-GXG2 performed well in a rabbit urinary infection model, inhibiting bacteria and preventing epithelial damage.

(4) The film-forming method's feasibility and flexibility were confirmed. The method was expanded to hernia mesh applications, developing a hydrophilic antibacterial patch (PU-GHB) with a one-step cross-linking process. PU-GHB effectively treated multidrug-resistant infections in a rat model without toxic effects.[2]

Key Words: Antibacterial, coating, polysaccharide, medical device

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Anti-ferroptotic injectable hydrogel microspheres

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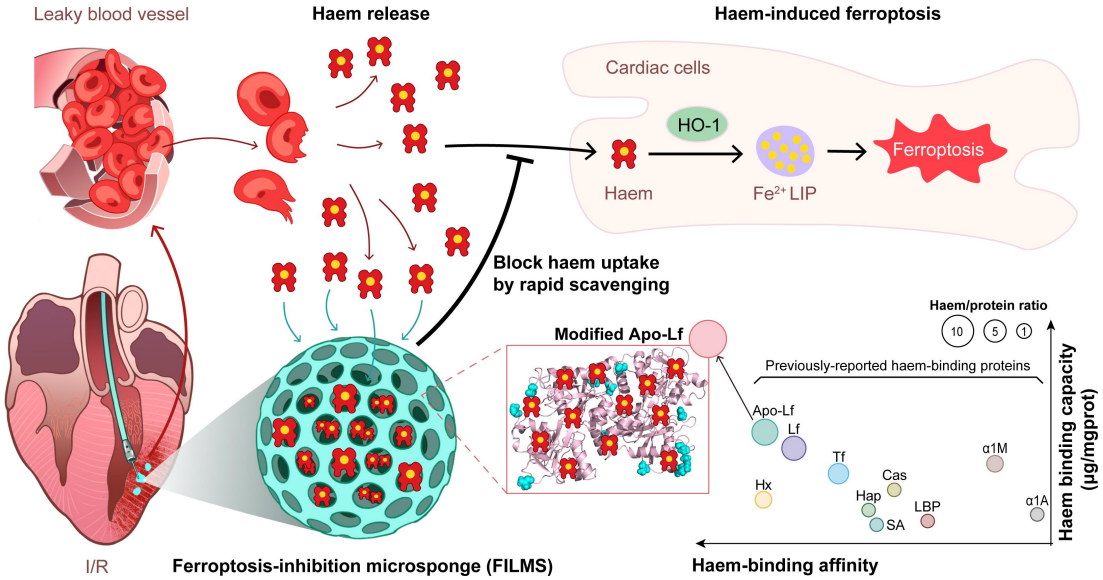
Introduction: Myocardial ischemia/reperfusion (I/R) injury is exacerbated by intramyocardial hemorrhage (IMH), which releases haem, a cytotoxic iron carrier that triggers ferroptosis. This study identifies haem as a key driver of cardiac damage and proposes intercepting its cellular uptake via localized haem-scavenging biomaterials.

Research Design: Methacryloyl-modified apo-lactoferrin (Apo-LfMA), derived from milk, was engineered to enhance haem-binding affinity (86% more sites, 10-fold higher affinity) and crosslinked into injectable microsponges (ALMS). ALMS were implanted into reperfused myocardium in rat and porcine I/R models to evaluate haem clearance, ferroptosis inhibition, and therapeutic outcomes.

Main Results and Discussion: ALMS rapidly sequestered extracellular haem in I/R-injured hearts, reducing myocardial iron levels and lipid peroxidation. In rats, ALMS decreased infarct size and preserved cardiac function. Porcine trials confirmed ALMS compatibility with transcatheter delivery and efficacy in reducing necrosis). Mechanistically, ALMS blocked haem-induced ferroptosis by preventing iron overload, as validated by transcriptomic and lipidomic analyses.

Conclusion: This study establishes haem scavenging as a novel strategy to mitigate I/R injury, demonstrating that ALMS, a milk-derived biomaterial, safely and effectively inhibits ferroptosis. The findings highlight the translational potential of implantable haem-binding devices for treating ferroptosis-related disorders.



Key Words: injectable hydrogel, ferroptosis, reperfusion injury, protein biomaterial

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Symposia 25

Tissue Engineering

Development of a PEG-CS Functional Coating Loaded with Sodium Tanshinone IIA Sulfonate for Small-Diameter Artificial Vascular Grafts

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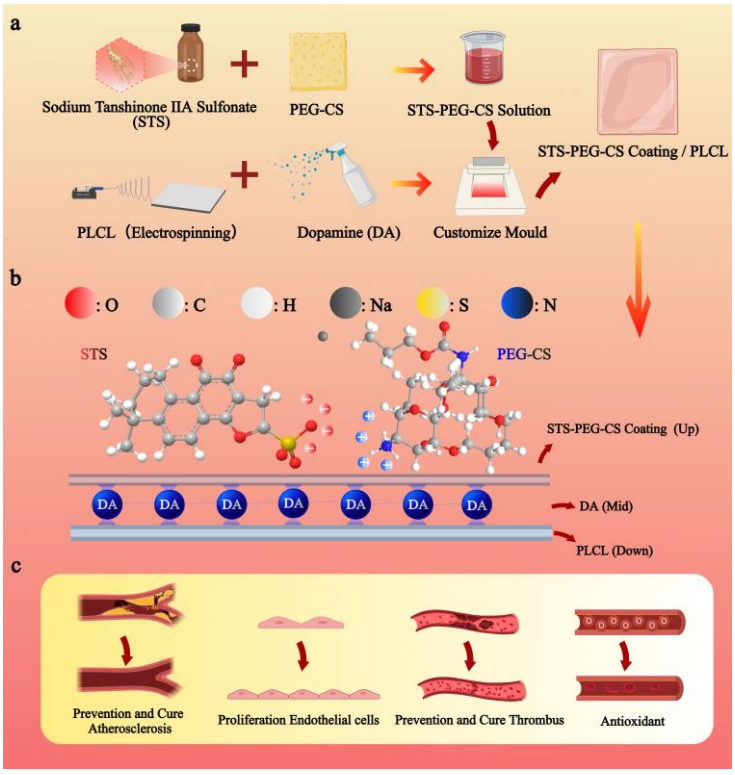
Abstract: The health of the vascular system is crucial for maintaining normal physiological functions in the body. However, factors such as chronic diseases and congenital defects often lead to impaired vascular function. Although autologous vessel transplantation and other treatment methods are currently used in clinical practice, the limited availability of donor vessels and associated trauma have led to the gradual adoption of artificial vascular grafts as alternatives. However, small-diameter artificial blood vessels often face issues such as thrombosis, neointimal hyperplasia, and long-term calcification after implantation, limiting their long-term patency. In this study, an artificial vascular scaffold was prepared based on poly(lactic acid)-poly(caprolactone) (PLCL) nanofiber membranes using electrospinning technology. A functional coating was constructed on its surface with a chitosan (CS) base grafted with polyethylene glycol (PEG), loaded with sodium tanshinone IIA sulfonate (STS). The hydrophilicity, mechanical properties, cytocompatibility, and anti-thrombosis performance of the coating were systematically evaluated by adjusting the PEG grafting degree (5%, 10%, 15%) and STS concentration (0.01%, 0.05%, 0.1%). The experimental results showed that the 15% PEG-CS coating exhibited the best biocompatibility and anti-platelet adhesion ability, while the STS-0.01 coating also demonstrated excellent anticoagulant and endothelialization-promoting properties in vitro. Animal experiments further confirmed that this coating had good biocompatibility and structural stability in vivo. In conclusion, the PEG-CS vascular scaffold coating loaded with sodium tanshinone IIA sulfonate developed in this study shows promising application prospects and is expected to provide a new approach for the clinical translation of small-diameter artificial vascular grafts.



Key Words: Sodium tanshinone IIA sulfonate; Polyethylene glycol; Coating; Artificial blood vessel

Acknowledgements: The authors acknowledge the support from the Science and Technology Commission of Jiaxing Program (2025CGZ020), and the National Natural Science Foundation of China (32071340).

Electrically Conductive and Anti-Inflammatory Hydrogel-Based Nerve Guidance Conduits for Enhanced Peripheral Nerve Regeneration

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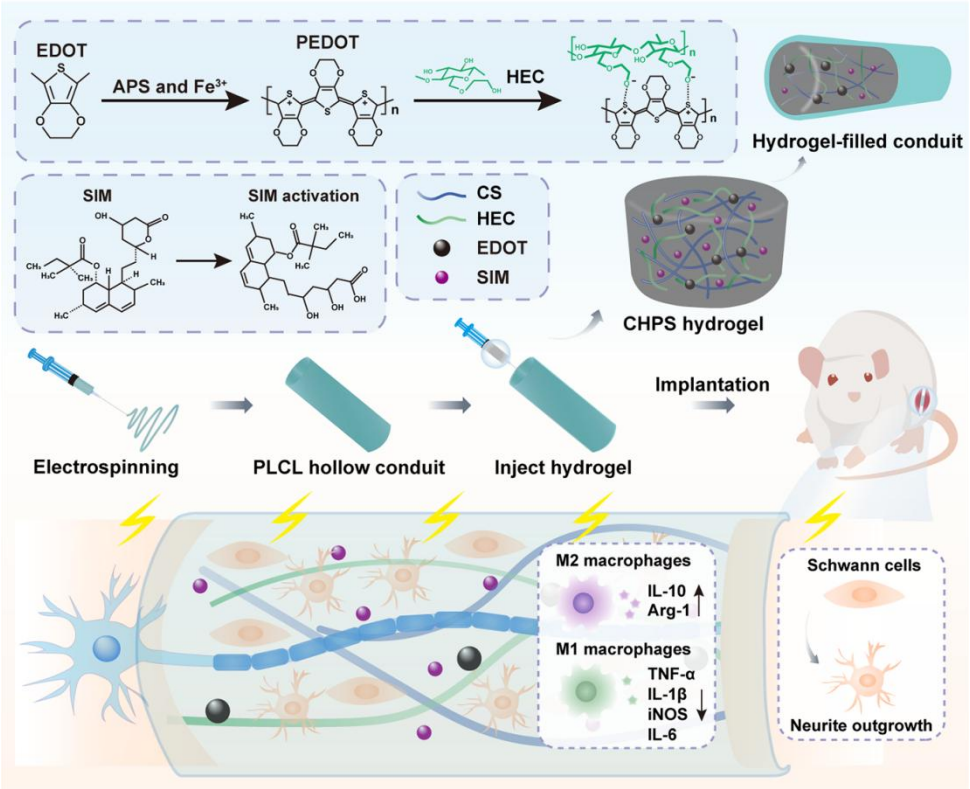
Nerve guiding catheters (NGCs) are crucial for peripheral nerve repair, providing physical guidance and establishing a conducive microenvironment to nerve regeneration. In this study, we developed a bifunctional CS-HEC@PEDOT/SIM (CHPS) hydrogel-filled electrospun polycaprolactone (PLCL) conduit. The hydrogel matrix was fabricated using chitosan (CS) and hydroxyethyl cellulose (HEC) as base materials. Conductive poly(3,4-ethylenedioxythiophene) (PEDOT) was synthesized in situ within the matrix to establish stable electrostatic interactions with HEC, enhancing its electrical conductivity. Additionally, anti-inflammatory simvastatin (SIM) was uniformly dispersed throughout the hydrogel network through optimized activation procedures. The CHPS hydrogel exhibited excellent electrical conductivity and sustained anti-inflammatory drug release. Comprehensive cellular and animal experiments demonstrated that CHPS hydrogel-filled conduits create an optimal environment for electrical conductivity and inflammatory control, effectively promoting sciatic nerve regeneration in rats and facilitating recovery of motor function and nerve conduction. In conclusion, this approach may offer substantial potential for advancing nerve repair strategies and inspiring developments in the clinical treatment of peripheral nerve injury.



Key Words: electrospinning; conductive hydrogel; anti-inflammatory drug

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Three-Dimensional Composite Aerogel Scaffolds based on Electrospun Poly(lactic acid)/Gelatin and Silica-Strontium Oxide Short Fibers Promote Bone Defect Healing

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Bone defect regeneration is a dynamic healing process, which relies on intrinsic ability of the body to repair albeit limited healing. The objective of this research was to synthesize hybrid scaffolds based on natural/synthetic polymers and inorganic nanomaterials (NMs). We prepared three-dimensional (3D) composite scaffolds based on flexible silica-strontium oxide (SiO_2-SrO) nanofibers and poly(lactic acid)/gelatin (PG) fibers. These scaffolds displayed an ordered porous structure as well as exhibited biocompatibility and biological activity. In vitro release studies demonstrated that the scaffolds enabled sustained and controlled release of silicon ions (Si^{4+}) and strontium ions (Sr^{2+}). Furthermore, these scaffolds not only upregulated the expression of osteogenic-related genes but also promoted tubule-like network formation in human umbilical vein endothelial cells (HUVECs) in vitro. The scaffold enabled concurrent bone regeneration and vascularization in rat skull defect repair. Taken together, our strategy of leveraging the synergistic effect of SiO_2-SrO short fibers and PG fibers may have potential to promote bone regeneration and potentially other bio-related disciplines.

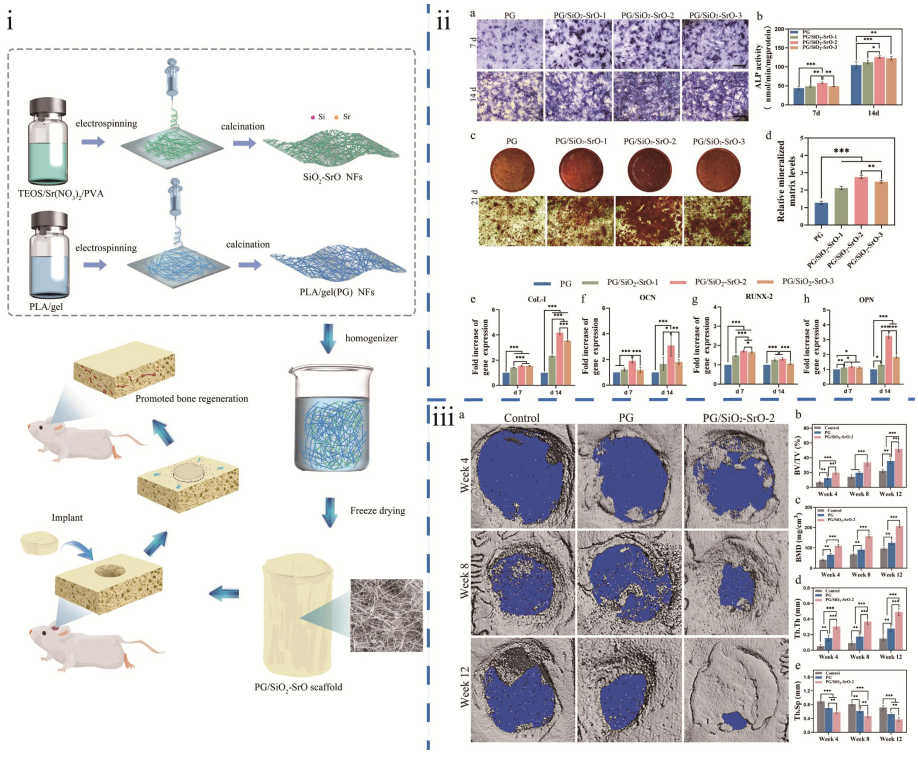

Figure. (i) Schematic diagram showing the fabrication of PG/SiO_2-SrO composite scaffolds for skull repair. (ii) *In vitro* osteogenic ability of composite aerogel scaffolds. (iii) *In vivo* bone regeneration by scaffolds in a rat cranial defect model.

Key Words: Inorganic nanofiber; Composite scaffold; Skull Repair; Electrospinning; Tissue engineering; Bone tissue engineering

Precision Endothelialization of Vascular Scaffolds via Bioorthogonal Chemistry

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Abstract: Artificial vascular graft is one of the main methods for the treatment of cardiovascular diseases. However, platelet activation and aggregation, immuno-inflammatory responses and smooth muscle cell proliferation will occur after implantation in human body. The promotion of rapid endothelialization of vascular scaffolds is the key to reduce thrombosis and intimal hyperplasia, thereby reducing restenosis and improving the therapeutic effect. In this study, polyurethane polymers containing amino groups were first synthesized and then fabricated into small-diameter artificial scaffolds via electrospinning technology, and bioorthogonal DBCO groups were grafted on the surface. Through the process of metabolic glycoengineering, azide (N_3) groups that could react specifically with DBCO groups were inserted on the surface of endothelial cells. The dynamic culture in vitro and simulation of dynamic circulation assay were performed, and with endothelial cells expressing different fluorescent proteins, it was proved that the N_3-engineered endothelial cells could selectively adhere to the surface of DBCO-modified vascular scaffolds, while the adherent cells could further proliferate to form a endothelial cell layer, which confirmed that the bioorthogonal reaction could successfully mediate the targeted adhesion of engineered endothelial cells to the vascular scaffold. Meanwhile, by introducing heparin and zwitterion multifunctional modifications, the constructed DBCO/PC/heparin multifunctional modified vascular scaffolds not only retained the selective cell adhesion mediated by bioorthogonal reaction, but also enhanced the anti-biofouling/anticoagulation performance and significantly reduced platelet adhesion. This project provides a promising idea for promoting precise and rapid endothelization of vascular scaffolds and a potential method to improve the long-term patency and therapeutic effect of vascular grafts.

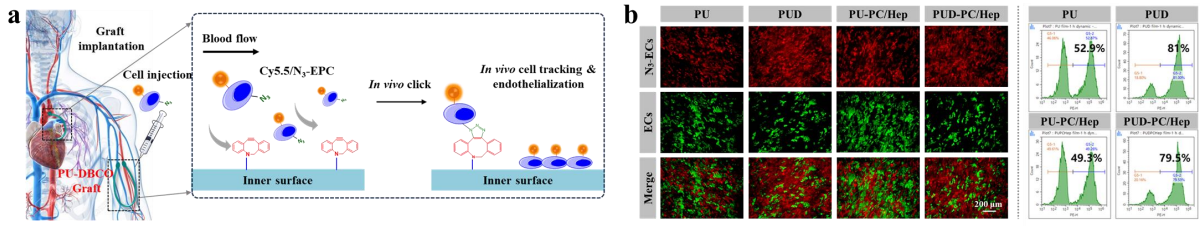

Fig.1 (a) The schematic illustration of the study (b) The cell adhesion on the graft surface and flow cytometry analysis after 1 h dynamic culture *in vitro* and 48 h proliferation.

Key Words: Vascular graft, Biorthogonal chemistry, Rapid endothelialization

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Multisite Captured Copper Ions via Phosphorus Dendrons Functionalized Electrospun Short Nanofibrous Sponges for Bone Regeneration

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Introduction

Metal ions are important trace elements in the human body, which have significant impact on normal life process, including maintaining life function, regulating metabolism, promoting tissue repair, and so on.[1] However, excessive metal ions can also cause certain damage to the human body. In this study, the electrospun short nanofibrous sponges (3D-NS) functionalized with phosphorus dendrons (3D-NS@PD) was innovatively constructed, which was capable of dynamically capturing free copper ions at multiple sites to realize the dynamic balance and physiological concentration of copper ions.

Research design

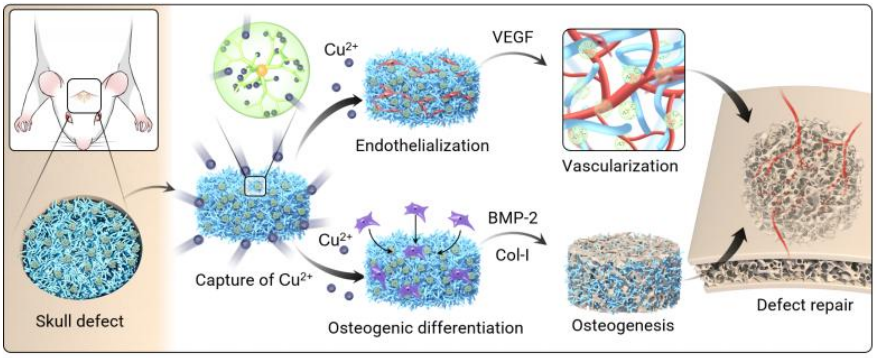
The electrospun short nanofibrous sponges (3D-NS@PD) with the ability to multisite captured copper ions were innovatively constructed by electrospinning, homogenization, and subsequent multifunctional modifications. It could capture free copper ions at multiple sites and stably release copper ions, which facilitated osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) and promoted the formation of new blood vessels.

Results and discussion

The phosphorus dendrons modified with pyrrole groups (PD) were grafted onto electrospun short nanofibrous sponges (3D-NS) *via* π-π conjugation to innovatively constructed the 3D-NS@PD, which can load and dynamically capture free copper ions at multiple sites, achieving the integrated repair of promoting vascularization and bone regeneration. The experiments confirmed that the 3D-NS@PD had good mechanical properties, water absorption, porosity and biocompatibility.

Conclusion

In this study, we prepared a PD functionalized micro-nano 3D-NS@PD, which could capture free Cu^{2+} to promote bone regeneration. The studies demonstrated this 3D-NS@PD could capture free Cu^{2+} at multiple sites and had good biocompatibility. Furthermore, the captured Cu^{2+} could accelerate osteogenic differentiation of BMSCs and blood vessel formation. This novel scaffold with the capacity of capturing metal ions at multiple sites, which provided a new strategy for bone regeneration and other tissue regeneration based on metal ions in the future.



Keywords: 3D short nanofibrous sponges, multisite capturing; copper ions, bone regeneration.

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Single-Atom Nanozyme Combining Bioactive Molecule in Hierarchical Microneedles for Spatiotemporally Treatment of Infected Diabetic Wounds

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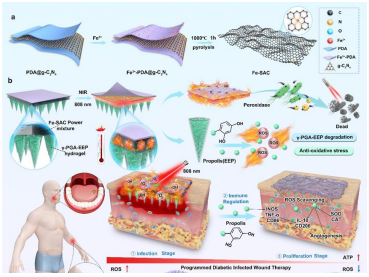
Abstract

Diabetic wounds struggle to heal due to high blood sugar, which fuels infections and inflammation. Effective healing requires balancing immune responses and energy metabolism. Researchers developed a microneedle patch (MN-FeSAC-PPE) with two components: iron-based nanozymes (FeSACs) in the base and propolis extract (PPE) in the tips. The FeSACs kill bacteria early using heat activated by light, while PPE reduces harmful oxidative stress. Together, they lower inflammation, boost cellular energy production, and accelerate tissue repair. Tests showed increased antioxidant enzymes (like Sod2, Gpx1) and decreased inflammatory markers (like TNF-α, IL-1β), improving healing by aiding blood vessel growth and skin regeneration. This dual-action patch offers a promising new treatment for infected diabetic wounds.



Keywords: FeSACs nanozymes, Microneedle, Antibacterial, Oxidative stress protection, Bioenergy metabolism, Immune homeostasis

Acknowledgements: This work was supported by the National Key R&D Program of China (2022YFE0123500), the National Natural Science Foundation of China (32201102 and 31771081), the Science and Technology Commission of Shanghai Municipality (22S31903300).

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Towards Next Generation Bioresorbable Implants

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Bioresorbable implantable medical devices are intended to facilitate regeneration of tissue using the body as a bioreactor. They and their metabolic byproducts are necessarily non-toxic and completely excreted. They are indicated for clinical problems presenting a defect of tissue that is large in volume, distributed in a challenging way, involves considerable donor morbidity for autologous reconstruction or introduces a high failure rate for alloplastic reconstruction. These are represented in several specific clinical contexts including large bone defects in the appendicular skeleton, bone defects of the craniofacial skeleton and breast volume replacement. Challenges in translation of bioresorbable implants include scaling up, hostile clinical environments (including infection and radiotherapy) and composite defects include whole organs.

The authors have undertaken large animal and clinical trials of implantable bioresorbable devices covering all of these clinical contexts. This presentation will present the contemporary science that informs future directions in bioresorbable devices. This includes never seen before results of systematic histological examination of explanted specimens and biopsies from animal and human studies that serve to outline the cellular processes involved in tissue regeneration. It also informs the next steps that should be taken to optimize next generation bioresorbable devices to improve the rapidity of tissue regeneration and work towards multi-phasic implants that are capable of regenerating multiple tissue types in a single device.

Key Words: bioresorbable, implant, reconstruction, defect

Bioelectronics for Tissue Engineering: A Review on Materials and Design Strategy in 3D

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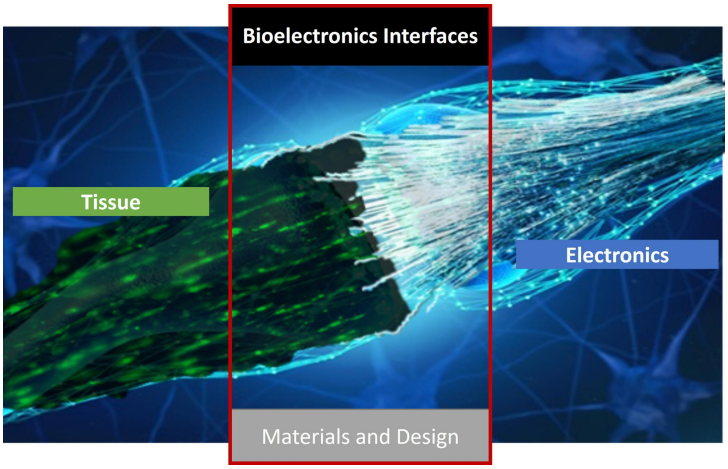
Bioelectronics is the area, which deals with interfacing electrical circuits with biological species. These electrical signals, if harnessed successfully, can be used to sense, stimulate, and regulate tissue's functions [1]. This will bring breakthrough discoveries in neurosciences, wound healing, musculoskeletal tissue engineering, cancer therapies and brain-computer interface research.

Ideally, the biomimetic tissue-electronics system should be formed as a continuum 3D matrix with fully integrated cell-materials-electronics components inside the continuum to capture the most accurate electrical events of the target tissue. New materials and design strategies are needed to assemble these bioelectronics interface, while bioprinting techniques provides the freedom to assemble different class of materials on-demand in 3D.

In this talk, we will present a state-of-the-art review on the materials and design strategy in creating new cell-electronics interfaces in tissue constructs. Future potentials of bioelectronics in tissue engineering will also be discussed [2].



Bioelectronics interfaces of cell and electronics within hydrogel matrix will drive new functions in tissue engineering.

Key Words: Tissue engineering, bioelectronics, bioprinting

Acknowledgements: This project is supported by NRF (award number NRF-NRFI07-2021-0007)

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Multilayer biomimetic scaffolds functionalized with stem cells-recruiting and angiogenic peptides for enhanced bladder regeneration

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Abstract: The complications of enterocystoplasy have challenged traditional bladder reconstruction methods[1]. Tissue engineering scaffolds, involving stem cells implantation and vascularization strategies, emerge as promising alternatives[2]. However, their applications are hindered by issues regarding the source of stem cells and the rapid loss of bioactive factors in a urinary environment. Here, multilayer biomimetic scaffolds consisting of polycaprolactone (PCL) nanofibrous mats and oxidized dextran/carboxymethyl chitosan hydrogel have been synthesized. Bone marrow homing peptide (BMHP) and vascular endothelial growth factor-mimicking peptide (VP) were incorporated to the hydrogel to recruit endogenous stem cells and promote vascularization, respectively. The results indicated that PCL mats not only reinforced the mechanical properties of composite scaffolds but also prolonged the retention of peptides via the hydrophobic surface. In vivo experiments demonstrated that BMHP and VP had crosstalk effects, amplifying their functions to accelerate bladder regeneration, enhance contractility of smooth muscle cells, inhabit fibrosis, and improve innervation. Overall, the novel functionalized scaffolds are potentially viable for urologic tissue reconstruction.

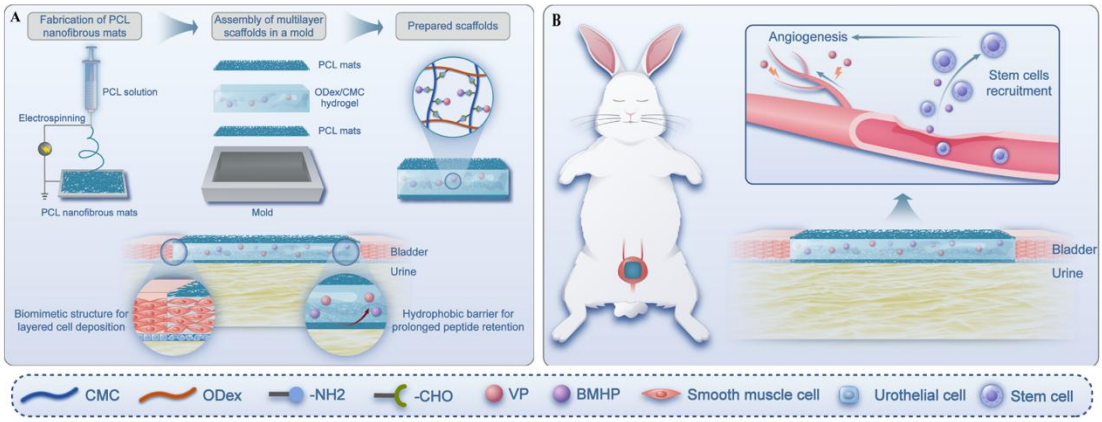

Fig.1. *Schematic illustration of this study. (A) Preparation of BMHP and VP-loaded multilayer scaffolds. (B) Implantation of the scaffolds and the crosstalk effects between BMHP and VP in vivo.*

Key Words: Bladder tissue engineering; Nanofiber/hydrogel composites; Layered structures; Endogenous stem cells; Vascularization.

Acknowledgements: This work was supported by the National Natural Science Foundation of China (82072823, 52173061, 51873157), Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant (20172019), Medical-Engineering Cross Project of Shanghai Jiao Tong University (YG2024ZD16), Pujiang Talent Program by Shanghai Science and Technology Commission (22PJ1405100), and Bethune Charitable Foundation (mnzl202012).

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Symposia 26

Tissue Repair Materials

Acceleration of Calvarial Bone Regeneration with A Multifunctional Hydrogel: Single-cell Transcriptome Analysis

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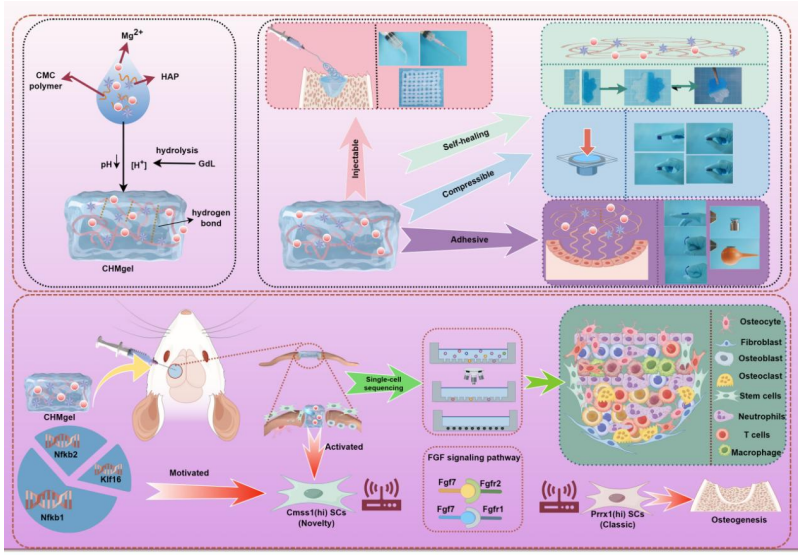
Introduction: Addressing the challenge of critical-size bone defect treatment, particularly in defects with irregular shapes, demands the development of innovative biomaterials. Hydrogels have received growing attention in bone regeneration, yet their physicochemical properties are often insufficient to meet clinical requirements.

Research design: In this study, we present the design of a multifunctional hydrogel, termed CHMgel, which integrates a physical carboxymethyl cellulose framework with hydroxyapatite (HAP) and Mg^{2+}.

Main resultss and discussion: Due to the formation of strong intermolecular hydrogen bonds, this hydrogel exhibits desirable properties such as injectability, high adhesion, satisfactory self-healing capacity, moderate mechanical strength, good biodegradability, and excellent biocompatibility. In-vivo testing in a rat model further demonstrates that CHMgel significantly enhances osteocyte accumulation and the formation of new lamellar bone. Single-cell RNA sequencing reveals that CHMgel treatment amplifies the proliferation of in situ stem cells, thereby accelerating bone regeneration. Importantly, Cmss1(hi) stem cells are markedly upregulated, influencing endochondral ossification through the elevated expression of key proteins such as Filip1l, Celf2, and Cmss1.

Conclusion: This study's cellular characteristics and interactions enhance our grasp of skeletal stem cell subsets in early biomaterial-aided bone regeneration, providing the basis for material strategies for osteogenesis control.



Key Words: scRNA-seq, multifunctional hydrogel, bone regeneration, stem cells, cranial defect

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An Artificial Piezoelectric-Conductive Integrated Peri-Implant Gingiva Enables Efficient Bacterial Inhibition and Soft-Tissue Integration

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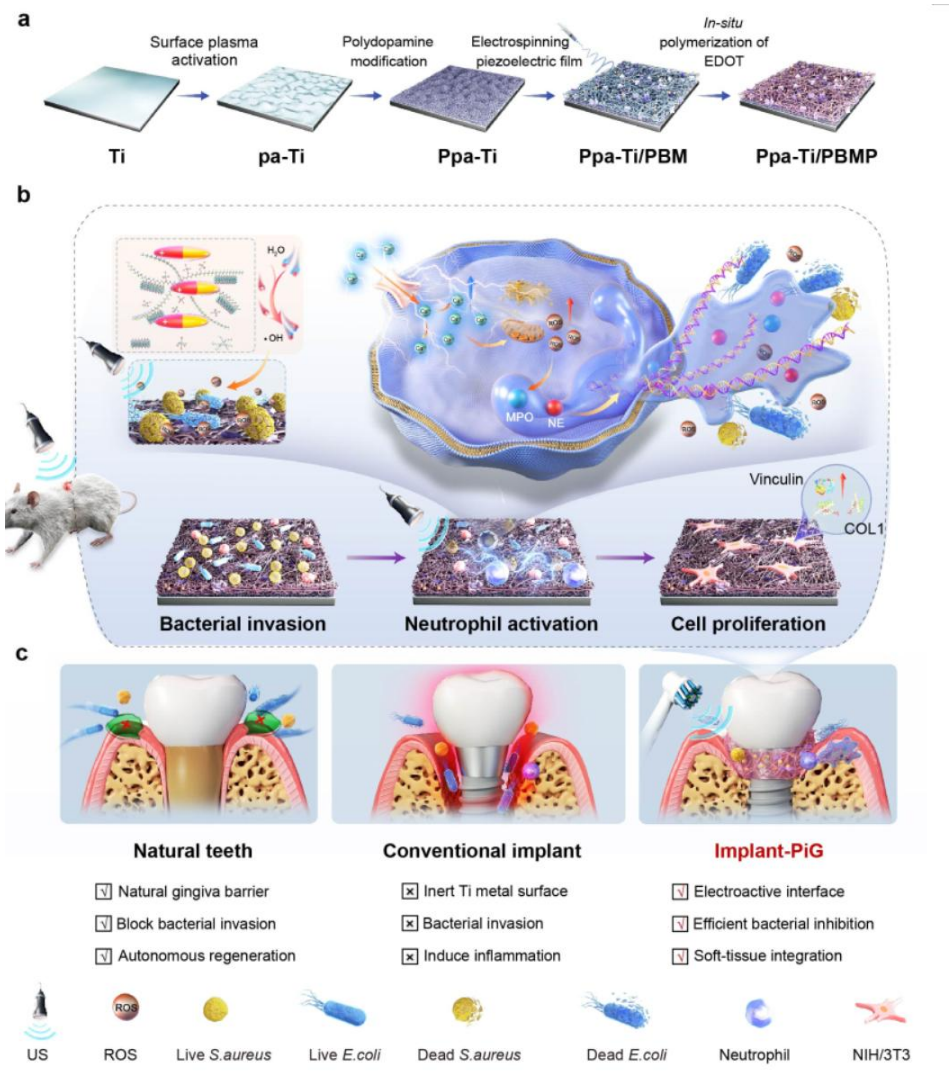
Abstract

Peri-implantitis is the main reason for dental implant failure. Optimizing electroactivity at the interface between dental implants and tissue is essential for enhancing integration and preventing bacterial invasion. Here, a bioinspired piezoelectric-conductive integrated peri-implant gingiva (PiG) with simultaneously enhanced antibacterial efficacy and soft-tissue integration is presented, which is based on a flexible piezoelectric film and conductive polymer network. The piezoelectricity of PiG is achieved through the electrospinning of polyvinylidene fluoride/BaTiO3/MXene on the polydopamine modified plasma-activated Ti surface, while the conductive property of PiG is achieved by the in-situ polymerization of 3,4-ethylenedioxythiophene monomers. Under ultrasonic irradiation, the PiG can promote the formation of neutrophil extracellular traps and reactive oxygen species, thus achieving a synergistic and efficient piezodynamic killing of Staphylococcus aureus (S. aureus) and Escherichia coli. Additionally, the piezoelectricity-enabled electrical stimulation endows the PiG with enhanced fibroblasts adhesion, proliferation, and collagen secretion. As a demonstration, ultrasound irradiation of PiG-grafted Ti implanted in a subcutaneous implantation rat model efficiently eliminates the S. aureus infection and rescues the implant with enhanced soft-tissue integration. The concept of an artificial PiG is anticipated to unlock new avenues for the development of high-performance implant materials, potentially extending their lifespans.



Keywords: MXene; Electrospinning; Piezoelectricity; Electrical stimulation; Implant-associated infections

Acknowledgements: This work was supported by National Natural Science Foundation of China (31771081, 52202108), National Key R&D Program of China Grants (2022YFe0123500), Science and Technology Commission of Shanghai Municipality (22S31903300), Fund of Shanghai Stomatological Hospital (SSH-2024-C01, SSH-2024-A01, SSH-2024-B02, SSH-2024-B06).

Targeted Macrophage CRISPR-Cas13 mRNA Editing in Immunotherapy for Tendon Injury

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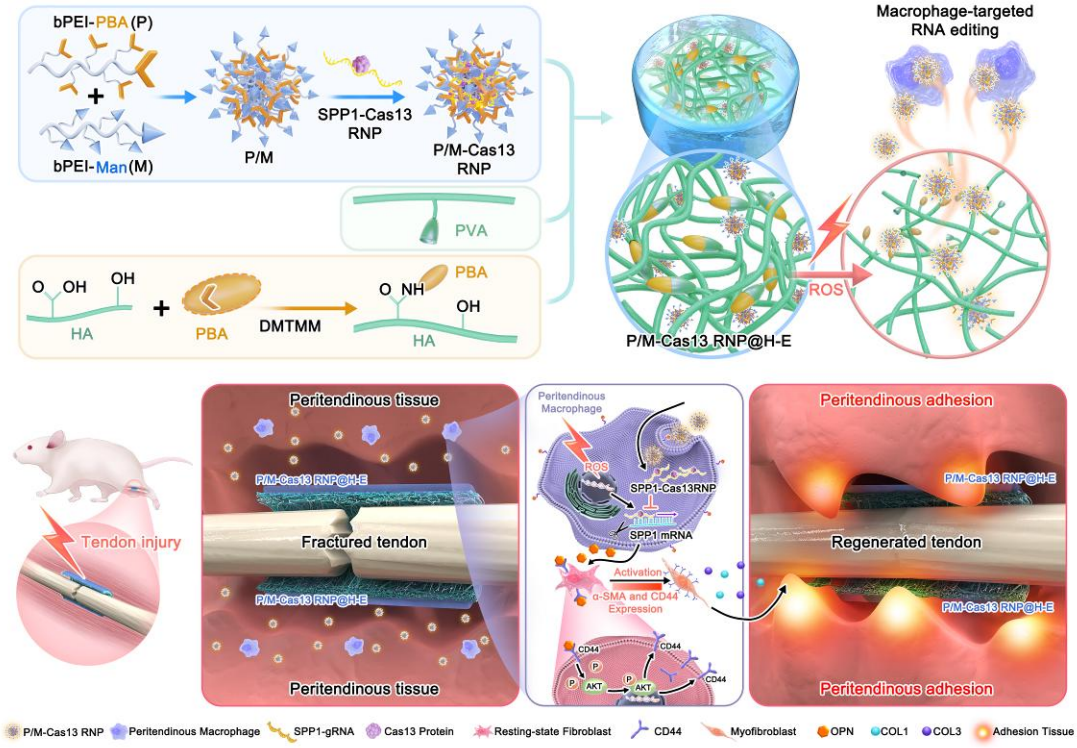
Introduction: CRISPR-Cas13 holds substantial promise for tissue repair through its RNA editing capabilities and swift catabolism[1]. However, conventional delivery methods fall short in addressing the heightened inflammatory response orchestrated by macrophages during the acute stages of tendon injury[2]. **Research design:** In this investigation, macrophage-targeting cationic polymers are systematically screened to facilitate the entry of Cas13 ribonucleic-protein complex (Cas13 RNP) into macrophages. **Main results and discussion:** SPP1 (OPN encoding)-producing macrophages are recognized as a profibrotic subtype that emerges during the inflammatory stage. By employing ROS-responsive release mechanisms tailored for macrophage-targeted Cas13 RNP editing systems, the overactivation of SPP1 is curbed in the face of an acute immune microenvironment. Upon encapsulating this composite membrane around the tendon injury site, the macrophage-targeted Cas13 RNP effectively curtails the emergence of injury-induced SPP1-producing macrophages in the acute This study furnishes a swift RNA editing strategy for macrophages in the inflammatory phase triggered by ROS in tendon injury, along with a pioneering macrophage-targeted carrier proficient in delivering Cas13 into macrophages efficiently.



Key Words: CRISPR-Cas13; Macrophage targeting; Tendon injury; Immunotherapy

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Spatial transcriptomic landscape unveils the critical dental follicle cell subset maintains the quiescence of replacement dental lamina

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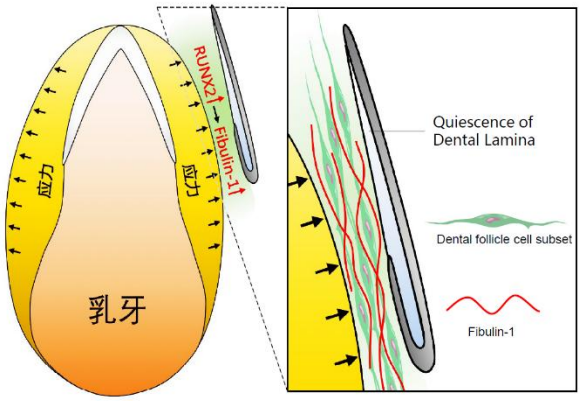
Abstract

Renewal of integumentary organs occurs cyclically throughout lifetime, but the mechanism that initiates each cycle remains largely unknown. In large mammals with diphyodont dentition, the replacement of deciduous teeth with permanent ones serves as a good model for studying ectodermal organ replacement. In this study, we described the landscape of cell subsets and microenvironment during the initiation and development of replacement permanent teeth at the single-cell transcriptome level. We found that the key dental follicle cell subset in the microenvironment maintains the quiescence of dental lamina progenitor cells and regulates their differentiation into most of the dental epithelium. We then elucidated the RUNX2-Fibulin1 pathway played the key critical role in this process.



Key Words: stem cell niche, homeostasis, tooth germ, dental lamina

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Early dental epithelial development and its role in multi-cusp molar morphogenesis

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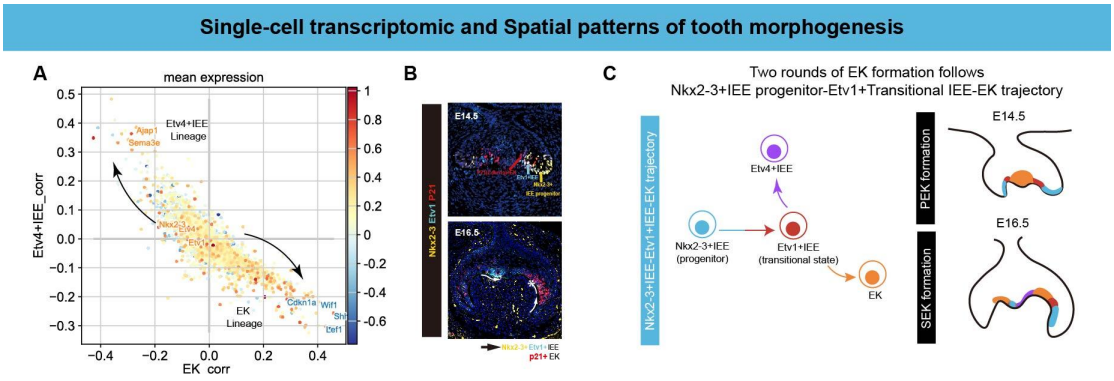
Tissue morphogenesis coordinates cell dynamics and fate specification[1]. Understanding how tissue morphogenesis is achieved remains a challenge. Tooth development is a crucial model for investigating tissue morphogenesis[2]. Recent work has shed light on how cell dynamics, including vertical telescoping migration, delamination et al., contribute to the cusps (peaks) and sulci (valleys) shape of tooth biting surface[3]. However, the molecular signature transition and fate specification during multi-cusps morphogenesis at cap-to-bell stage of tooth development remain unclear. Here using scRNA-seq and explant-based lineage tracing, we show that multiple rounds of non-proliferative signaling center (enamel knot) formation direct multiple cusps (peaks) shape of molar tooth. Each round of enamel knot formation is through Nkx2-3+IEE progenitor-Etv1+transitional IEE-EK trajectory. Etv1+ transitional IEE have two-directional differential potential, one is non-proliferative EK and another is proliferative Sema3e+IEE. And the sulci (valley) deepens between cusps relying on Sema3e+IEE proliferation. Together these findings revealed how tooth epithelial cells specify their fates and how fate specification influence the characteristic biting-surface shape of tooth.



Key Words: tooth development, tissue morphogenesis, enamel knot, and dental epithelial trajectory

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Polyphenol/Metal Ion Mediated Macrophage Metabolism Reprogramming to Promote Wound Repair

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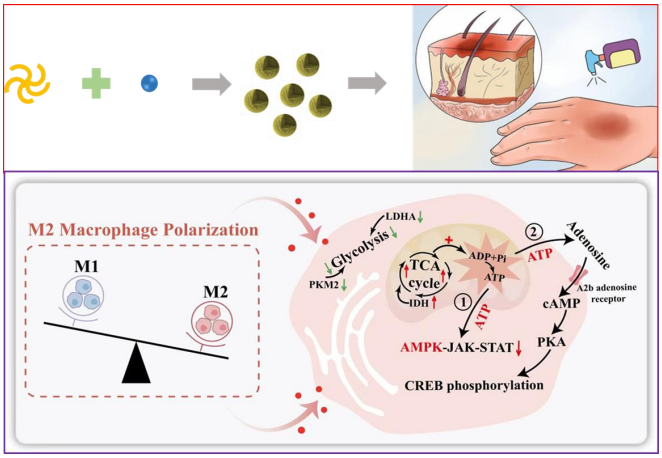
Chronic wound healing is a major challenge in clinical treatment, and its core mechanism is closely related to macrophage polarization disorder. Due to excessive activation of glycolysis, pro-inflammatory M1 macrophages continue to accumulate. The mitochondrial oxidative phosphorylation of anti-inflammatory M2 is severely hindered. The metabolic immune imbalance leads to uncontrolled inflammation, interruption of tissue repair signals, ultimately prolonging wound healing time. Therefore, the development of biomaterials with immune metabolism regulation for the treatment of burn wounds has important research significance.

Tannic acid/manganese ion complex (TA/Mn) was synthesized through molecular self-assembly. Then it was cultivated with macrophages to evaluate the polarization and metabolic reprogramming through biological methods. The mechanism of energy metabolism regulation of macrophage polarization was revealed through combined analysis of gene-metabolomics. Finally, a deep second-degree burn animal model was used to verify its repair effect and explore the specific mechanism.

Our results show that TA/Mn can target macrophage mitochondria to enhance IDH and SDH enzyme activity by adjusting spatial conformation, and then restore the metabolic pathway of tricarboxylic acid cycle (TCA) to improve mitochondrial oxidative phosphorylation levels. The energy metabolism of macrophages is reprogrammed to produce more ATP. On the one hand, ATP can regulate macrophage polarization through the AMPK-JAK-STAT axis. On the other hand, ATP is converted into adenosine for extracellular release, activating the cAMP PKA CREB axis to promote M2 polarization, thereby regulating the inflammatory microenvironment and ultimately accelerating burn wound repair.

TA/Mn can regulate macrophage polarization from M1 to M2 through energy metabolism reprogramming, then promote the healing of deep second-degree burn wounds. This research achievement will provide new strategies for the clinical treatment of chronic wounds through metabolic regulation.



Key Words: Chronic Wounds, Metabolism, Immune Regulation, Tannins

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Autonomous Biomaterials for Precision Bone Repair: Mechanisms, Applications, and Future Directions

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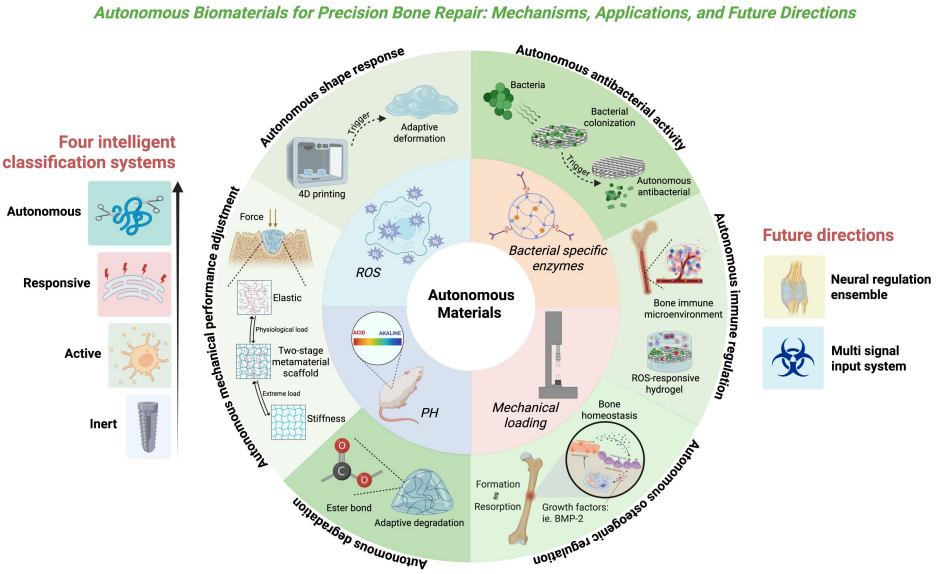
Bone defect repair from trauma, tumors, and infections remains a critical challenge in global medical research, with traditional biomaterials constrained by mismatched degradation rates, poor immune microenvironment adaptation, and delayed infection responses. In contrast, autonomous biomaterials, as an emerging category, overcome the passive nature of conventional materials through dynamic feedback mechanisms and intelligent design, offering novel solutions for precision bone regeneration. This review synthesizes recent advances in autonomous biomaterials for precision bone repair over the past five years, based on the four-tier intelligent classification system (inert, active, responsive, autonomous). These materials actively sense and regulate complex physiological environments via pH, reactive oxygen species, mechanical stimuli, and bacterial enzyme-triggered responses, enabling autonomous shape adaptation, dynamic antibacterial activity, immunomodulation, osteogenic control, degradation matching, and mechanical property modulation. Future research directions emphasize neural regulation-integrated materials and multi-signal input systems, which are poised to shift bone repair strategies from replacement therapies to in situ regenerative paradigms, thereby providing a novel material foundation for precision medicine. While still in early development, autonomous biomaterials demonstrate compelling potential to address complex defect challenges through precision environmental responsiveness. A deeper understanding of autonomous biomaterials in confronting bone defect complexities could unlock breakthroughs in this field.



Key Words: Autonomous biomaterials, Precision bone repair, Dynamic feedback, Intelligent materials

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A PCL/HAp/GO Composite Scaffold with Time-Sequenced Release of Angiogenic and Osteogenic Bioactive Components for Critical-Sized Bone Defect Repair

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In this study, we developed a sequentially bioactive polycaprolactone/hydroxyapatite/graphene oxide (PCL/HAp/GO) composite scaffold via 3D printing and freeze-drying for critical-sized bone defect repair. The scaffold featured a mechanically robust PCL/HAp framework with a GO/gelatin matrix, enabling controlled angiogenic (GO) and osteogenic (HAp) factor release. Biological efficacy was systematically evaluated through in vitro assays using rat retinal microvascular endothelial cells (rRMECs) and bone marrow stromal cells (rBMSCs), complemented by in vivo assessment in a rat calvarial defect model. *In vitro* evaluations revealed that PH/GO-1 (1% GO) significantly enhanced endothelial cell migration and angiogenesis ($p < 0.001$) via the HIF-1α/VEGFA pathway, while also promoting osteogenesis by elevating ALP activity, calcium deposition, and upregulating osteogenic markers like RUNX2 and OCN. The *in vivo* results at 12 weeks confirmed the scaffold's therapeutic efficacy, with a BV/TV ratio of 32.16% and a BMD of 0.49 g/cm³ ($p < 0.01$), indicating enhanced vascularization and mineralized matrix deposition. The scaffold's time-sequenced design enabled early GO-induced angiogenesis and sustained HAp-mediated osteogenesis, synergistically promoting bone regeneration. These findings underscore the scaffold's potential for clinical translation, offering a novel strategy that integrates mechanical stability with bioactivity for effective bone defect repair.

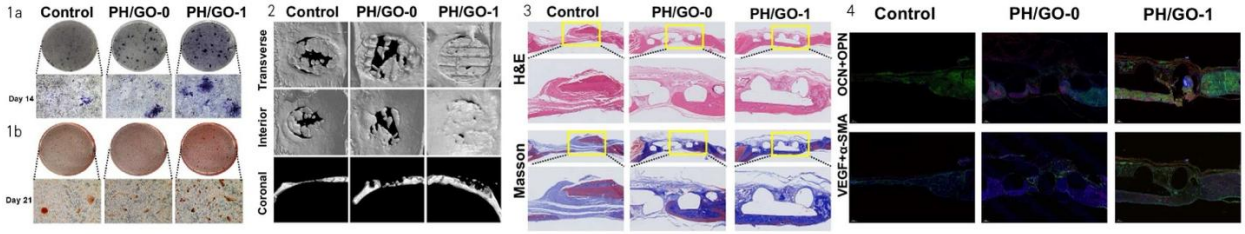

FIG 1 (a) Alkaline phosphatase (ALP) activity in the PH/GO−1 group was significantly higher than that in the CON and PH/GO−0 groups at day 14 of osteogenic induction. (b) Alizarin Red S (ARS) staining revealed greater calcium deposition in PH/GO−1 compared to controls at day 21, indicating enhanced osteogenic mineralization.
FIG 2 Three−dimensional Micro−CT analysis of new bone formation across transverse, interior, and coronal planes revealed that PH/GO−1 exhibited extensive neobone coverage at 12 weeks post−implantation, nearly completely filling the defect region, which was significantly greater than that observed in both the CON and PH/GO−0 groups.
FIG 3 H&E and Masson's staining at 12 weeks: PH/GO−1 exhibited near−complete defect closure with enhanced neobone deposition and scaffold degradation.
FIG 4 Immunofluorescence at 12 weeks: PH/GO−1 exhibited dense osteogenic signals (OCN+OPN) and enhanced vascularization (α−SMA+ VEGF) versus CON/PH/GO−0.

Key Words: bone tissue engineering, 3D printing, graphene oxide, angiogenesis, bone regeneration

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