Poster Session Notes

1. Display

Please locate and mount your poster at **Cheng Yu Tung (CYT) Building 1/F Lobby poster area** according to your assigned poster number.
To qualify for judging, your poster must be mounted before **12:30 p.m. on January 10th**. The display board is available since 8:30 a.m. on January 10th

2. Retrieval

Please take down and retrieve your poster before **12:30 p.m. on January 11th**. The organizer is not responsible for any posters left after this deadline.

No.	Name	Institute	Title
1	Che-Ming Hu	Academia Sinica	Augmenting Clonal Expansion with Polymerized Cellular Taxidermy for Personalized T Cell Therapy
2	Claudia Vazquez Pereira	DTU - Technical University of Denmark	Mycelium–Cellulose Hydrogels from Medicinal Mushrooms as Bioactive Drug-Delivery Platforms
3	Nuzzo Domenico	National Research Council of Italy	Green Biofabrication of New Plant-Derived Nanovesicles: Sustainable Carriers for Functional Biomaterial Innovation
4	Yue Zhang	Westlake University	Programming Signaling Hotspots on Immune Cell with Engineered Ligand Clusters
5	Yongcheng Chen	Zhejiang University	Side-Chain Engineering of NIR-II-Emissive Aggregation-Induced Emission Luminogens to Boost Photodynamic and Photothermal Antimicrobial Therapy
6	Zuolong Liu	Zhejiang University	A D-Zwitterionic Polypeptide Platform for Lysosomal Escape and Stealth Delivery of Therapeutic Enzymes
7	Picone Pasquale	National Research Council of Italy	Biofabrication of Vesicles from Isolated Mitochondria: A New Perspective for Brain Mitochondrial Transplantation
8	Xin Tang	University of Florida	Decoding Hidden Forces behind Human Cancer: Breaking New Grounds in Mechanosensitive Long-Distance Intercellular Waves and Networks
9	Zhengwei Mao	Zhejiang University	Living Microbes/Nanozymes Biohybrids for Disease Treatment
10	Wenqi Yang	Dalian University of Technology	Biophysical Insights into the Effects of Alkyl Glucoside Surfactant Structural Characteristics on Antigen Stability Under Thermal and Mechanical Stress
11	Yishu Wang	Institute of Process Engineering, Chinese Academy of Science	Microreactor RBC Ghosts Deliver Camptothecin for Tumor Immunotherapy
12	Wenjing Wang	Institute of Process Engineering	Selenized Neural Stem Cell-Derived Exosomes: a Neotype Therapeutic Agent for Traumatic Injuries of the Central Nervous System
13	Lihao Ji	Nanjing university	A Live Biohybrid Bacterial Therapy Based on Engineered Serratia Marcescens
14	Liang Wang	HKUST	Bifunctional Ultrasound-Controllable β-Gly Nanopatch for TBI Repair
15	Yi Liu	Beihang University	Nanomaterial-Genetics Enables Receptor-Guided Targeting of Ligand-Functionalized Nanoparticles for Cell-Type–Specific Neuromodulation
16	Yu-shuan Chen	Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan	Formulation-Driven Brain Targeting: Mechanistic Insights and Therapeutic Applications
17	Kelong Fan	Institute of Biophysics, Chinese Academy of Sciences	Nanozymes Expanding the Boundaries of Biocatalysis
18	Hui Wei	Nanjing University	Biomimetic Nanozymes for Hard-to-Treat Inflammatory Disease Therapy
19	Qifeng Guan	Beihang University	Micropore Structure Engineering of Injectable Granular Hydrogels via Controlled Liquid-Liquid Phase Separation Facilitates Regenerative Wound Healing in Mice and Pigs
20	Juyeon Kim	Sungkyunkwan University	Robust Protein-Engineered Porous Architectures for Biomimetic Alveolar Tissue and Lung-on-a-Chip Platforms
21	SooJung Chae	Sungkyunkwan University	Engineering an Ex Vivo Pancreas–Myosteatosis Muscle Tissue via Biofabrication
22	GaEun Heo	Sungkyunkwan University	Mushroom Chitosan–Collagen Bioink and Comb-Integrated Bioprinting for Bone–Tendon Interface Regeneration
23	Fangfu Ye	Institute of Physics Chinese Academy of Sciences	Extracellular Matrix-Regulated Microglial Migration and Neuron Self-Organization
24	Xiuyuan Luo	Beihang University	Viscoelastic Silk Cryogels for Bone Tissue Regeneration
25	Yilin Zhang	Beihang University	Janus Silk-based Patch with Temporary Adhesion for Inflammatory Mediators Removal in Corneal Alkali Burn Treatment
26	Wenbo Zhang	Beihang University	Silk-Based Multilayer Coatings for Anticoagulation and Durability
27	Peng Yu	South China University of Technology	Semiconductor Biomaterials for Tissue Regeneration
28	Hongxu Lyu	Shanghai Institute of Ceramics, Chinese Academy of Sciences	Silicate Biomaterials-Induced Bone Marrow Organoids for Tissue Regeneration
29	Chengtie Wu	Shanghai Institute of Ceramics, Chinese Academy of Sciences	3D Printing of Biomimetic Biomaterials and Transformation
30	Chuntae Kim	Pusan National University	Enhanced Cardioprotection via Modulation of Epithelial–Mesenchymal Transition by Cell-Clustering Biosynthetic Phages
31	Tae-Hyung Kim	Sungkyunkwan University (SKKU)	Stimuli-Responsive Nanopattern Platforms for Autonomous Stem Cell Differentiation
32	Changshun Ruan	Shenzhen Intitutes of Advanced Technology	Full Organ Manufacture: Parallel Coaxial Printing for Multiscalar Circulation System
33	Xingyu Chen	Southwest Jiaotong University	Study on Tissue Repair Biomaterials Adapted to Pathological Microenvironment
34	Yidian (Henry) Xu	Sydeney University	Nanoparticle Mediated Dox-iron Target Therapy Wiping out Malignant Stem Cells in Blood Cancer
35	Dohyun Kim	Yonsei University College of Dentistry	Fibronectin-Guided Immune-Stromal Cell Crosstalk Promotes Angiogenesis in Pulp-Dentin Complex Regeneration
36	Xuemin Liu	East China University of Science and Technology	Crowding as a design lever: Tuning Collagen (I) Fibrillogenesis and Bioactivity via Crowder Library
37	Xinyue Ning	Sun Yat-sen University	Research on Three-Dimensional Porous Scaffold Materials with Mechano-Electrical Response
38	Angelina Mao	Cloumbia University	Targeted Delivery of SSRIs via Nanoparticles for SERT Modulation in the Gut Epithelium
39	Xinyu Liu	Peking University	Construction of self-assembled protein-polymer conjugates for enamel repair
40	Jae-Hyeon Lee	Konkuk University	CARRIER-FREE Nano-anticoagulant Based on a Low Molecular Weight Heparin-Lipid Conjugate with Albumin-mediated Shuttling
41	Gayong Shim	Soongsil University	Environment Responsive Nanoplatforms for Targeted Cancer Therapy
42	Dongpyo Kim	Harbin Institute of Technology, Shenzhen	Combinational Prodrug Nanotherapy Validated In a Brain Organoid Model of Alzheimer's Disease
43	Jiaqi Xu	University of Chinese Academy of Sciences	In Vivo Macrophage Reprogramming via Biomimetic Membrane Protein Transfer Nanotechnology
44	Xilong Wu	Hainan University	Multi-Physical-Field Driven Smart Nanozymes for Precision Medicine Diagnosis and Therapy
45	Hao Zhang	Nanjing Agricultural University	An Orally Administrated Platform for Targeted Therapy of Inflammatory Bowel Disease
46	Bing Jiang	Zhengzhou University	Precision Regulation of Nanozyme Activity: From Structural Design to Therapeutic Translation

47	Liang Luo	Huazhong University of Science and Technology	A Completely Degradable Polydiacetylene Prodrug Enables Months-Long Combination Therapy for Osteoarthritis
48	Dan Shao	Sichuan University	High-throughput Design of Hemoperfusion Platform for Selective Capture of Neutrophil Extracellular Traps in Severe Sepsis
49	Mingxuan Zhang	The Eighth Affiliated Hospital of Sun Yat-sen University	uPAR-Targeted Nanoparticles Delivering Senolytic Drugs (D&Q) Attenuate Vascular Calcification through Selective Clearance of Senescent Cells
50	Jiang Yang	Sun Yat-sen University	Nerve Growth Factor-Targeting Nanocluster-Antibody-Drug Conjugates for Intravesical Precision Theranostics of Interstitial Cystitis
51	Zhihui Liang	Dalian University of Technology	Engineered Design of Aluminum Salt-Based Nanoadjuvants and Mechanistic Understanding of Their Immunological Potentials
52	Ani Chi	South China University of Technology	Local Inhibition of NLRP3 in Testicular Macrophages Rejuvenates Male Reproductive and Physical Function in Aging Mice and Cynomolgus Macaques
53	AL-AMMARI Abdulrahman Ali Mohammed	The Chinese University of Hong Kong	Transition Metal-Based Nanozyme Platforms for Alleviating Atherosclerosis via Oxidative Stress Modulation
54	Jing Ruan	Shanghai Jiao Tong University School of Medicine	Photothermally Enhancing Cancer Radio-immunotherapy via Impairing Intracellular Lactate and DNA Damage Repair
55	Yi Wang	Hong Kong Baptist University	Applications of Zein-Based Nanomaterials in Biomedical and Food Fields
56	Sungyeong Kim	Technical University of Denmark	Bifunctional Hydrogel Microneedle Patch for Glucose Sensing and Transdermal Drug Delivery with Potential Applications for Diabetes Management
57	Bo Xiao	University of Electronic Science and Technology	Oral Silk Protein-Adjuvanted Nanovaccines Target Intestinal Lymph Nodes to Simultaneously Activate Systemic and Mucosal Immunity Against Colon Cancer
58	Rong Zhang	Hebei medical university	Engineered Exosomes Delivering miR-218-5p Attenuate Environmentally-induced Pulmonary Fibrosis Progression by Targeting Ferroptosis-driven Epithelial-Mesenchymal Transition
59	Peipei Jin	The First Affiliated Hospital of University of Science and Technology of China	Development of a Nano-Targeting Chimera for the Degradation of Membrane and Cytoplasmic Proteins
60	Yangzi JIANG	The Chinese University of Hong Kong	Development of Small Peptides for Regulating NGF Signalling and Bone Regeneration
61	Dong-Wook Han	Pusan National University	pVIII Engineered Filamentous Phages Trigger High Avidity Clustering and MSC Mechanotransduction for Stage Specific Immune Control in Diabetic Peripheral Neuropathy
62	Tingbin Zhang	Hebei University of Technology	Design New Magnetic Nanoparticles for in Vivo Dynamic Regulation of Mitochondrial Function
63	Ding Ding	Shanghai Jiao Tong University	Translational Research on Functional Nucleic Acid-Based Theranostics
64	Xiaoyi Zhao	Beijing University of Chemical Technology	A Circuit-Inspired Paradigm for Programming Biological Processes with Modular Nanomaterials
65	Liyang Zhou	Shanghai Jiao Tong University	Mitochondrial Metabolism-Reprogrammed Nanodrug to Enhance Tumor Cuproptosis
66	Kang Moo Huh	Chungnam National University	Potent and Safe Cancer Vaccine via a 'Minimal Toxicity Core-Maximum Stability Shell' NanoPlatform
67	Yu Gao	Technical University of Denmark	Biodegradable Enzymatic Fuel Cells for Intestinal Glucose Sensing and Controlled Drug Release
68	Jaeseong Lee	Soongsil University	Organ targeted cationic lipid nanoparticles engineered through microfluidics for nucleic acid delivery
69	Wei Wei	Nanjing University	Exploring the Versatile Roles of Inorganic Polyphosphate Materials in Biological Systems
70	Juan Li	Ningbo Institute of Materials Technology & Engineering, Chinese Academy of Sciences	Chiral Neuropeptide Bioprobes -Design and Application
71	Xiaoxiang Ren	Shanghai University	Porosity-Programmed Haversian-like Bone Organoids with Emergent Vascular-Osteogenic Coupling
72	Huining He	Tianjin Medical University	Surface Charge of Lipid Nanoparticles Governs Stress Granule-Mediated Immune Enhancement

Poster Session Notes

1. Display

Please locate and mount your poster at **Cheng Yu Tung (CYT) Building 1/F Lobby poster area** according to your assigned poster number.
To qualify for judging, your poster must be mounted before **5:00 p.m. on January 11th**. The display board is available since 10:00 a.m. on January 11th

2. Retrieval

Please take down and retrieve your poster before **6:00 p.m. on January 12th**. The organizer is not responsible for any posters left after this deadline.

No.	Name	Institute	Title
1	Kai Wang	Beihang university	Ultrafast and Dilution Resistant In-Situ Gelation Hydrogel Platform via a Molecularly-Engineered Oxime-Crosslinking
2	Xin Zhang	Peking University Third Hospital	Biodegradable Piezoelectric Conductive Composite Hydrogel
3	Qihang Zhang	The Chinese University of Hong Kong	Quantitative Phase Imaging Promoting Cell Biology, Biomedicine, New Materials and Beyond
4	Kexin Zhang	HKUST	Field-Modulated Nanoconfinement Strategy for Controlled Phase Crystallization of Glycine toward Biofunctional Piezoelectric Materials
5	Guosheng Song	Hunan University	In Vivo Molecular Imaging Based on Responsive Magnetic Probes
6	Kemeng Xiao	Shenzhen Institute of Advanced Technology , CAS	Bioelectronic Coupling for Solar-Powered Biosynthesis in E. coli
7	Cheng Jiang	The Chinese University of Hongkong (Shenzhen)	Functional Materials Based Platform for Harvesting and Probing Extracellular Vesicle Subpopulation toward Decoding Degenerative Disease
8	Ho-pui Ho	The Chinese University of Hong Kong	Pyramidal Sub-Nanometer Oxidised Nanopore: a New Device Platform for Single Nucleotide/Amino Acid Sequencing
9	Caixia Yin	Shanxi University	An Innovative Approach for Specific Fluorescent Labeling of Norepinephrine in Situ
10	Baisong CHANG	Wuhan University of Technology	Second Near-Infrared (NIR-II) Phosphorescence Imaging
11	Wu Yuan	The Chinese University of Hong Kong	Telerobotic OCT imaging guided interventions in dynamic luminal organs
12	Yuan Yao	Westlake University	3D Printing of High-Performance Hydrogel Bioelectronic Implants
13	Wen Sun	Dalian university of Technology	Photoresponsive Dyes for Biological Applications
14	Shu XIAO	The Hong Kong Polytechnic University (PolyU)	Simultaneous Profiling of Surface Protein and miRNA in Single Extracellular Vesicles via DNA-Walker/CRISPR
15	Hsien-Ming Lee	Academia Sinica	Peptidyl Liposome for Trigger-Responsive Delivery Vesicle and Smart MRI Contrast
16	Mu Jing	The Chinese University of Hong Kong, Shenzhen	NIR-II Fluorescence Imaging: Targeting Optimization and Biomedical Applications
17	Yutong Wang	Tsinghua University	MRI-compatible flexible neuroelectronics with bio-adaptive interfaces for brain spatiotemporal analysis at ultra- high magnetic fields
18	Yifan Shang	Hunan University & The Chinese University of Hong Kong	scMIR: A vision–language foundation model for single-cell light microscopy image representation
19	Baiyan Xiao	Peking University	Harnessing Toroidal Topology to Regulate Force-Electric Properties and Promote Bone Formation in Biomimetic Nanocomposite Membranes
20	Lin Wang	Huazhong University of Science and Technology	An Implantable and Degradable Silk Sericin Protein Film Energy Harvester for Next-Generation Cardiovascular Electronic Devices
21	KiSu Kim	Pusan National University	Kirigami Upconversion Photodynamic Dressing for Antibiotic-Free Control of MDR Wound Infections
22	Zhou Liu	Shenzhen University	Frequency-encoded hydrogel robots for multiplexed magnetic control
23	Hui Zhao	The Chinese University of Hong Kong	Design and implementation of a hyperglycemia-sensing switch for precise glucose regulation
24	Yang Jiao	Dalian University of Technology	Architecture of Supramolecular Probes and Their Biological Applications
25	Nana Zhao	Beijing University of Chemical Technology	A Closed-Loop Theranostic Probiotic Platform for AI-Powered Home Management of Inflammatory Bowel Disease
26	Chen Liu	Hebei medical university	The NMD3-PARP1 Positive Feedback Loop Drives Therapy Resistance in Colorectal Cancer Through Enhanced DNA Damage Repair
27	Yun Kong	The Eighth Affiliated Hospital of Sun Yat-sen University	Vaccine-Induced CD8+ T Cells Mediate Targeted Immunotherapy of Medial Vascular Calcification
28	Jiezhao Zhan	South China University of Technology	Self-Activating Nanoagents for Precise Antibacterial and Antitumor Therapy
29	Anwei Zhou	Nanjing University	Bioengineered Neutrophils for Intelligent Infection Control
30	Fei Jin	The Chinese University of Hong Kong	Ultrasound-Activated Wireless Electrical Vagus Nerve Stimulation for Treating Enteritis
31	Calista Calista	Tsinghua University	The Development of Silica-Based Delivery RNAi Therapy for Primary Hyperoxaluria (PH)
32	Xuequan ZHOU	Tsinghua University	Photobiological Applications of Supramolecular Metallophilic Interactions
33	Liqiang ZHOU	University of Macau	Rewriting Cancer Immune Cycle with Engineered APC-Like Neutrophils Optimizing Antigen Presentation in Genetic Immunotherapy
34	Yanbin Chen	Institute of Radiation Medicine Chinese Academy of Medical Science & Peking Union Medical College	A Radiotherapy-Responsive Peptide Hydrogel for Pulsatile Release of mRNA-LNPs Synergizes with Immune Activation to Prevent Breast Cancer Recurrence
35	Zheng Wang	Huazhong University of Science and Technology	A NIR Light-Driven Transformable Liquid Metal-Based Nanovaccine for Inhibiting Postoperative Colorectal Cancer Recurrence
36	Choi Chung Hang Jonathan	The Chinese University of Hong Kong	Barrier-Penetrating Bioactive Small Gold Nanoparticles Enter Challenging Disease Sites and Alleviate Chronic Diseases
37	Xin Zhou	The First Hospital of Hebei Medical University	A Brush-Like Dual-Adjuvant M13 Nanovaccine Against Avian Influenza Infection
38	Kanghyeon Kim	Korea University	Reversible Manipulation of the Hierarchical Ligand Anisotropy for Macrophage Regulation
39	Nayeon Kang	Korea University	Mathematical Modeling of Ligand Networks for Reversible Cell Response
40	Yuri Kim	Korea University	Submolecular-Level Dynamic Engineering of Ligand Nanostructure for Macrophage Immunoregulation
41	Sungkyu Lee	Korea University	Versatile Engineering of Ligand Spacing on Self-Assembly to Regulate Stem Cell Differentiation
42	Hyunsik Hong	Korea University	Dynamic Control of Liganded Nanogeometry for Cellular Regulation
43	Chowon KIM	Korea University	Graph Theory-Based Mathematical Modeling of Nanoligand Networks Regulating Reversible Stem Cell Fate
44	Bingbing Sun	Dalian university of Technology	Liver-Targeting mRNA Vaccine Ameliorates Pollen Allergy by Enhancing Regulatory T Cell Induction
45	Karim Kazi Neha	Imperial College London	Glycoconjugate Production in Liposome
46	Jiajia Xue	Beijing University of Chemical Technology	Gradient hydrogel–nanofiber nerve guidance conduit with multiple inductive cues promotes peripheral nerve repair in primate models
47	Han Chang Kang	The Catholic University of Korea	Redox-Disrupted Diselenide Polymersomes for Tunable Organelle Targeting and Therapeutic Synergy
48	Pham Yen Khang	Soongsil University	Synthesis and Characterization of Porphyrin-Based Nanomaterials for Catalytic Cancer Therapy

49	Ji Hoon Jeong	Sungkyunkwan University	Chemoimmunological Intervention of Crosstalk between Tumor Microenvironment and Draining Lymph Node for Improved Cancer Immunotherapy
50	Meiwan Chen	University of Macau	Dual-pathway STING Nano-agonist Featuring Immunosuppressive Microenvironment Reprogramming for Hepatocellular Carcinoma Therapy
51	Shalik Ram Joshi	Hanyang University	A Skin-Compatible and Photothermally-Activated Electronic Tattoo for Depth-Tunable Transdermal Drug Delivery
52	Yun Chang	The Hong Kong Polytechnic University	Engineered Immunotherapies for Precise Disease Management
53	Hon Fai Chan	The Chinese University of Hong Kong	A Human Stem Cell-based 3D Microphysiological Platform for Skeletal Muscle Disease Modeling and Therapeutic Discover
54	Dai Fei Elmer Ker	The Hong Kong Polytechnic University (PolyU)	Multi-Targeting of Injured Rotator Cuff Muscle-Tendon Units with Fit Muscle-Tendon Graft
55	Yingheng Liu	The University of Hong Kong	Precision Robotic Fabrication of Anti-fibrotic Biointerfaces for Maxillofacial Implant Integration
56	Zhong (Alan) Li	The Chinese University of Hong Kong	Chiral Nanoparticles Drive Enantiomer-specific Osteogenesis and Accelerate Stem Cell-based Bone Regeneration
57	Dahee KIM	Korea University	Magnetically Switchable Nanoscale Groove-Ridge Biointerfaces for Dynamic Stem Cell Regulation and Translational Bone Regeneration
58	Jichuan Qiu	Shandong University	Piezo-Anchored Hydrogels for Neural Stem Cell Delivery and Brain Injury Repair
59	Jing Zhu	The Chinese University of Hong Kong	From Monolayers to Multilayers: Faraday Wave Bioassembly for Advanced Osteochondral Tissue Engineering
60	Yewen Zhu	Hangzhou Normal University	Multifunctional Strontium Phosphate Silicate Scaffolds: 3D-Printed Osteogenic Solution for Bone Defects
61	Song Yaping	Shandong University	Dual-Mode Antibacterial ZIF8-Inspired Orthopedic Implant Nanocoating for Biofilm elimination and Osseointegration
62	Ronghang Chang	East China University of Science and Technology	Structural regulation and medical applications of collagen
63	Yifeng Wang	Guangzhou Medical University	Bio-Nano Recognition Mechanism of Nanostructures with Cellular Membrane
64	Chun Kit Kwok	The Chinese University of Hong Kong	Live-Cell Tracking of Specific RNA G-Quadruplex for Stress Sensing by L-RNA Fluorogenic Bifunctional Aptamer
65	Jie Lin	Ningbo Institute of Materials Technology & Engineering, CAS	Selectivity and Stability Reshaping High-Sensitivity Detection Boundaries -Semiconductor SERS Nanobiosensor
66	Tao Yue	Jiangsu University	Temporal-Guided Dynamic Cell Segmentation
67	Limin Jin	Peking Union Medical College	TH1 cell-mediated immune reprogramming for vessel normalization
68	Tianhui Chen	Fudan University	Reprogramming of iPSCs to NPCEC-like cells by biomimetic scaffolds for zonular fiber reconstruction

Augmenting clonal expansion with polymerized cellular taxidermy for personalized T cell therapy

Che-Ming J. Hu[1*]

[1]Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

Adoptive T-cell therapies are limited by unreliable identification and expansion of rare tumor-reactive T cells (TRTs), largely due to antigen instability and rapid tumor cell lysis during co-culture. We developed taxidermic clonal augmentation (TCA), a biomaterials-driven strategy using polymerized tumor cells (PTCs)—tumor cells photo-crosslinked into nonviable, solid-state antigen-presenting scaffolds that stably preserve native immunopeptidomes. PTCs resist lysis, maintain intact MHC-I complexes, and support sustained, antigen-specific T-cell expansion without genetic modification. Across EG7-OVA and clinically relevant, weakly immunogenic tumor models, TCA selectively amplified antigen-specific $CD8^+$ T cells while minimizing nonspecific proliferation. PBMCs from tumor-bearing mice expanded with PTCs yielded enriched TRT populations that, upon adoptive transfer, significantly improved tumor control. We further show platform applicability with clinical biopsies. These findings position TCA as a materials-enabled, antigen-agnostic platform for scalable TRT discovery and personalized T-cell therapy development.

MYCELIUM–CELLULOSE HYDROGELS FROM MEDICINAL MUSHROOMS AS BIOACTIVE DRUG-DELIVERY PLATFORMS

Cláudia V. Pereira[1], Khorshid K. Guyan[1], Morten B. Svendsen[1], Anja Boisen[1]

[1]Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics (IDUN), Department of Health Technology, Technical University of Denmark, Lyngby, Denmark

In drug delivery, there is a growing demand for sustainable and biocompatible materials that combine structural performance with therapeutic function. Here, we describe composite hydrogels obtained by incorporating in vitro-grown mycelia from medicinal fungi, such as *Hericium erinaceus* (Lion's Mane), *Ganoderma lucidum* (Reishi), and *Schizophyllum commune* (Split Gill), into cellulose-based matrices functioning as bioactive carriers for therapeutic use.

Species-specific mycelia were cultivated directly within cellulose mixtures in custom-designed molds, enabling the fungal network to form and integrate with the cellulose matrix. Characterizations of morphology, mechanical behavior, and in vitro cytocompatibility were completed for the mycelium-cellulose composites. Initial results show low cytotoxicity and that adhesion and stiffness vary among fungal species, suggesting the composite can be tuned for different release targets and applications.

The mycelium–cellulose composites also contain naturally occurring β-glucans and polysaccharides that may contribute to intrinsic biological activity. Drug encapsulation and release studies are ongoing to evaluate their suitability as delivery platforms. After release, the matrix is expected to undergo natural biodegradation and fermentation processes, reducing persistence within the body.

Altogether, this work aims to position mycelium as a fully biodegradable and functional component for drug delivery systems, providing a more sustainable alternative to conventional synthetic polymers.

GREEN BIOFABRICATION OF NEW PLANT-DERIVED NANOVESICLES: SUSTAINABLE CARRIERS FOR FUNCTIONAL BIOMATERIAL INNOVATION

Domenico Nuzzo[1], Laura Palumbo[1], Antonella Girgenti[1], Loredana Abbate[2], Angela Carra[2], Pasquale Picone[1]

[1]Institute for Biomedical Research and Innovation, National Research Council, Via U. La Malfa 153, 90146 Palermo, Italy. [2]Institute of Biosciences and Bioresources, National Research Council, Via U. La Malfa 153, 90146 Palermo, Italy

Nanotechnology and nanomedicine represent transformative frontiers in the treatment of human diseases, with plant-derived nanovesicles emerging as eco-friendly, biocompatible carriers for bioactive phytomolecules and therapeutics. Although extracellular vesicles offer high potential as delivery systems, their isolation suffers from non-standardized protocols, low yields, and high plant material consumption, limiting scalability. Conversely, Vesicles obtained through Tissue Disruption (VTDs) enable bulk production but yield heterogeneous mixtures contaminated by cell wall debris and extracellular matrix components, resulting in variable size, composition, and bioactivity across batches. Our patented technology (PCT/IB2025/051717) introduces an innovative platform for the production of uniform plant cell–derived nanovesicles (Phyto-NanoVes), designed to overcome the main challenges related to variability, scalability, and sustainability in conventional processes. Starting from the isolation of plant cells and their subsequent *in vitro* expansion, it is possible to generate nanovesicles with well-defined physicochemical properties using optimized and reproducible protocols. Phyto-NanoVes are derived from a controlled, expandable, cryopreservable, and easily engineerable cell pool, ensuring batch-to-batch consistency while minimizing waste. By identifying the phytocomplex or natural molecule of interest and selecting the plant species and tissues most enriched in that compound, it is possible to isolate cells and produce nanovesicles enriched with the desired bioactive. Recent studies highlight the therapeutic promise of nanovesicles in antiviral applications (e.g., via specific viral binding, enhanced delivery of antiviral phytocompounds and mRNA vaccines across mucosal barriers, and immune modulation to inhibit infection and trigger neutralizing responses) yet highlights the need for standardized sources to advance clinical translation against viral threats like SARS-CoV-2. Our innovation facilitates drug loading (e.g., antivirals) for targeted delivery, while supporting nutraceutical fortification and drug formulations. This scalable, low-cost approach harnesses nature's nanoscale engineering capabilities and paves the way for next-generation, sustainable nanotherapeutics with tunable bioactivity. *Project: INF-ACT, Spoke 1 (P.P.) and Spoke 5 (D.N.). Project number PE00000007, CUP B53C20040570005.*

PROGRAMMING SIGNALING HOTSPOTS ON IMMUNE CELL WITH ENGINEERED LIGAND CLUSTERS

Yue Zhang[1,2], Han Fu[1]

[1]Material Science and Engineering, School of Engineering, Westlake University, Hangzhou, Zhejiang Province, China.
[2] School of Life Science, Westlake University, Hangzhou, Zhejiang Province, China.

Immune cell recognition is governed by the nanoscale spatial organization of membrane receptors into signaling hotspots. While manipulating this organization is a promising strategy for controlling immune activity, it has been hindered by the limited ability to engineer corresponding ligand arrangements with nanoscale precision. Here, we report a biomimetic bead platform that enables the controlled display of nanoscale ligand clusters. Using the "don't eat me" signal CD47, we demonstrate that these engineered clusters profoundly enhance inhibitory signaling. Beads presenting clustered CD47 resist macrophage phagocytosis for ~1.5 hours in vitro, whereas controls with non-clustered CD47 are internalized within 0.5 hours. Mechanistically, this enhancement is rooted in the multivalent engagement of SIRPα into inhibitory signaling hotspot, leading to its accelerated recruitment, enhanced ITIM phosphorylation, and a subsequent blockade of actin remodeling and integrin activation. These molecular-level disruptions translate to a 50-fold reduction in macrophage capturing forces, as measured by optical tweezers. Furthermore, following peritoneal injection in mice, beads with clustered CD47 exhibit significantly reduced phagocytosis in vivo. Finally, we demonstrate the therapeutic potential of our platform in a murine model of pathological red blood cell clearance, showing that CD47-clustered beads effectively inhibit the phagocytosis of stressed erythrocytes. Our work establishes the therapeutic capacity of engineered ligand clusters to modulate immune signaling hotspots, offering a promising strategy for treating disorders driven by aberrant phagocytosis, such as macrophage activation syndrome-associated anemia.

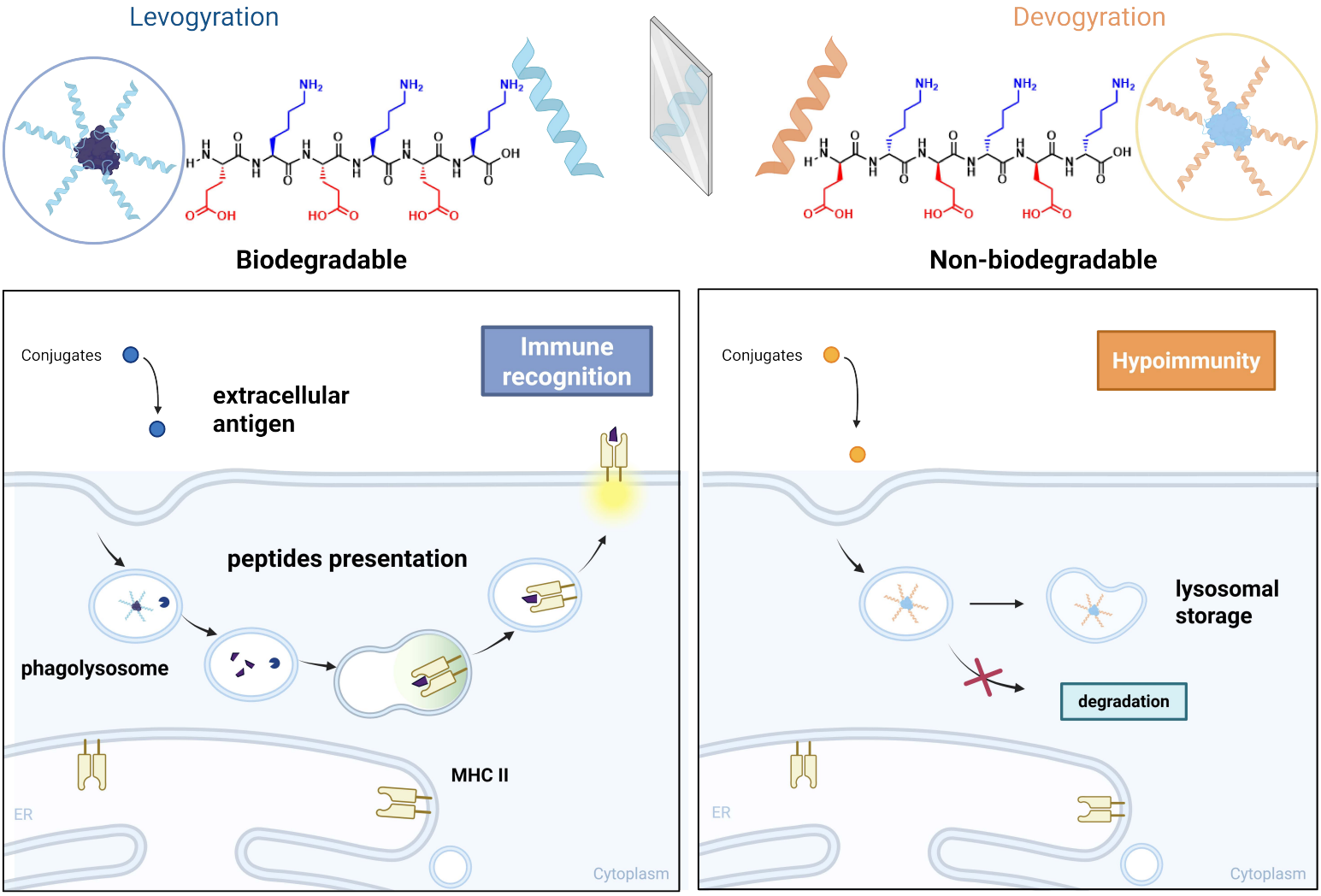
Side-Chain Engineering of NIR-II-Emissive Aggregation-Induced Emission Luminogens to Boost Photodynamic and Photothermal Antimicrobial Therapy

Yongcheng Chen[1], Qiao Jin[1]*

[1]MOE Key Laboratory of Macromolecule Synthesis and Functionalization, Department of Polymer Science and Engineering, Zhejiang University, Hangzhou 310058, P. R. China

Abstract

Immune cell recognition is governed by the nanoscale spatial organization of membrane receptors into signaling hotspots. While manipulating this organization is a promising strategy for controlling immune activity, it has been hindered by the limited ability to engineer corresponding ligand arrangements with nanoscale precision. Here, we report a biomimetic bead platform that enables the controlled display of nanoscale ligand clusters. Using the "don't eat me" signal CD47, we demonstrate that these engineered clusters profoundly enhance inhibitory signaling. Beads presenting clustered CD47 resist macrophage phagocytosis for ~1.5 hours in vitro, whereas controls with non-clustered CD47 are internalized within 0.5 hours. Mechanistically, this enhancement is rooted in the multivalent engagement of SIRPα into inhibitory signaling hotspot, leading to its accelerated recruitment, enhanced ITIM phosphorylation, and a subsequent blockade of actin remodeling and integrin activation. These molecular-level disruptions translate to a 50-fold reduction in macrophage capturing forces, as measured by optical tweezers. Furthermore, following peritoneal injection in mice, beads with clustered CD47 exhibit significantly reduced phagocytosis in vivo. Finally, we demonstrate the therapeutic potential of our platform in a murine model of pathological red blood cell clearance, showing that CD47-clustered beads effectively inhibit the phagocytosis of stressed erythrocytes. Our work establishes the therapeutic capacity of engineered ligand clusters to modulate immune signaling hotspots, offering a promising strategy for treating disorders driven by aberrant phagocytosis, such as macrophage activation syndrome-associated anemia.


Levogyration
Devogyration
Biodegradable
Non-biodegradable
Conjugates
extracellular antigen
Immune recognition
peptides presentation
phagolysosome
MHC II
ER
Cytoplasm
Conjugates
Hypoimmunity
lysosomal storage
degradation
ER
Cytoplasm

BIOFABRICATION OF VESICLES FROM ISOLATED MITOCHONDRIA: A NEW PERSPECTIVE FOR BRAIN MITOCHONDRIAL TRANSPLANTATION

Pasquale Picone[1], Antonella Girgenti[1], Laura Palumbo[1], Gokhan Burcin Kubat[2,3], Ibrahim Turkel[4], Domenico Nuzzo[1]

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Mitochondrial activity is essential for higher brain functions, and its impairment has been associated with a wide range of neurological disorders. Growing evidence indicates that mitochondria, or their components, can be physiologically released from one cell and subsequently taken up by another, including neurons, astrocytes, and microglia in the central nervous system. This intercellular transfer contributes to the regulation of multiple biological processes, including cellular bioenergetics.

Mitochondrial transplantation has recently emerged as an innovative therapeutic strategy aimed at transferring healthy mitochondria into cells or tissues with mitochondrial dysfunction to restore cellular function and promote tissue repair. However, its application to the central nervous system remains limited by the presence of the blood–brain barrier, low cellular uptake efficiency, and the lack of specific targeting.

To address these challenges, we have developed an *innovative biofabrication protocol* for the production of vesicles derived from isolated mitochondria, specifically designed to enhance the delivery of functional mitochondrial components to the brain.

These vesicles (~100 nm in diameter) maintain a membrane potential comparable to intact mitochondria, contain active mitochondrial proteins and enzymes. Moreover, preliminary data indicate their ability to cross an *in vitro* model of the blood-brain barrier and are efficiently taken up by brain cells.

Such features make these vesicles an innovative and scalable platform to overcome the current limitations of brain mitochondrial transplantation.

DECODING HIDDEN FORCES BEHIND HUMAN CANCER: BREAKING NEW GROUNDS IN MECHANOSENSITIVE LONG-DISTANCE INTERCELLULAR WAVES AND NETWORKS

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Electrically excitable cells such as neurons and muscles transmit long-distance calcium or electrical signals to regulate their physiological functions, such as brain-wide computation and body-scale motion. While the molecular underpinnings and down-stream effects of these intercellular communications in electrically excitable cells have been well appreciated, little is known about whether and how electrically non-excitable cancer cells spontaneously initiate and transmit long-distance intercellular signals. Recently we discover that non-excitable human colon and prostate epithelial cancer cells spontaneously initiate and spread long-distance intercellular calcium waves in acute tumor slices and synthetic hydrogel platforms. Importantly, the spatial-temporal characteristics of these biochemical waves can be tuned by the different mechanical stiffnesses of cellular microenvironments. Xenograft model studies suggest that these calcium signals promote the growth rate of tumors in mice. Further, pharmacological studies identified that the inositol-trisphosphate-receptor (IP_3R)-regulated calcium release from endoplasmic reticulum (ER), which is activated by the G_q-PLC-IP_3R pathway, is a major cause for the initiation of spontaneous calcium transients. In this talk, we will present the detailed functional characterization and molecular mechanism of this unique mechano-regulated biochemical wave. Our results provide evidence that mechanosensitive calcium dynamics enables long-distance functional communication in non-excitable cancer cells and offer the potential of modulating multiscale calcium signalling for next-generation cancer therapies.

Living microbes/nanozymes biohybrids for disease treatment

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Key words: biohybrids, nanomedicine, microbe, biomedical applications

Abstract of the talk: Living microbes characterized by distinctive biological functions including specific targeting, gene invasion, immune modulation, and so forth have been receiving intensive attention from researchers worldwide owing to their promising potential for producing numerous theranostic modalities against diverse pathological conditions. Nevertheless, concerns during applications, such as rapid immune clearance, altering immune activation modes, insufficient gene transduction efficiency, and so forth, highlight the crucial issues of excessive therapeutic doses and the associated biosafety risks. To address these concerns, synthetic nanomaterials featuring unique physical/chemical properties are frequently exploited as efficient drug delivery vehicles or treatments in biomedical domains. Researchers nowadays can create adaptable living microbe-based nanohybrids that not only overcome the limitations, but also combine the benefits of natural substances and nanotechnology to produce novel and promising therapeutic agents. We will discuss the fundamental physiochemical properties of the microbes, and briefly outline the basic construction methodologies of these hybrids. We will then emphasize their distinct therapeutic performances for various diseases.

Photograph and Biography of the invited speaker:

Zhengwei Mao is now a Professor and Chair in the Department of Polymer Science and Engineering at Zhejiang University. He received his Ph.D. at Zhejiang University in the field of materials science and had a postdoc experience at the Max Planck Institute of Colloids and Interfaces, Germany. His research is focused on polymeric biomaterials and seeks to control the microstructure of materials for the purpose of manipulating the responses of cells and tissues, with the application for cancer therapy and tissue regeneration. He now serves as one of the editors of Acta Biomaterialia.

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Biophysical Insights into the Effects of Alkyl Glucoside Surfactant Structural Characteristics on Antigen Stability Under Thermal and Mechanical Stress

The stability of protein antigens during production, storage, and transportation is critical for determining the effectiveness and safety of vaccines. However, protein antigens are susceptible to thermal and mechanical stresses, which can lead to aggregation and decreased immunogenicity. This study utilized alkyl glucosides to analyze the relationship between the structural characteristics of alkyl glucosides and their effects on the biophysical properties of proteins by using antigens, including bovine serum albumin (BSA), human papillomavirus virus-like particles (HPV VLPs), and tetanus toxoid (TT), through comprehensive biophysical analysis. Among the surfactants tested, N-dodecyl-β-D-maltoside (MalC12), with its longer hydrophobic chain and dual-sugar headgroup, was particularly effective in preserving antigen stability. MalC12 formed a dense protective layer through hydrophobic interactions, reducing heat-induced aggregation and maintaining the proteins' secondary structures. Under mechanical stress, MalC12 decreased protein adsorption at interfaces, minimized the risk of protein unfolding, and enhanced hydrophobic interactions with the proteins. In an HPV vaccine model, MalC12 effectively preserved HPV immunogenicity by preventing thermal-induced aggregation. These findings highlight the importance of surfactant characteristics in preventing protein destabilization and offer valuable insights for designing excipients that enhance antigen stability and immunogenicity in vaccine formulations.

MICROREACTOR RBC GHOSTS DELIVER CAMPOTHECIN FOR TUMOR IMMUNOTHERAPY

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The clinical potential of camptothecin analogs is limited by their poor solubility and the drawbacks of existing delivery systems, such as low drug loading and significant toxicity. To overcome these challenges, we developed a novel biomimetic platform leveraging the long-circulating "stealth" properties of red blood cells (RBCs).

This study presents the first construction of chimeric camptothecin nanocrystalline nano-erythrocytes (nRBC@HCPT). RBC vesicles were prepared via a hypo-osmotic and iso-osmotic process to remove hemoglobin. Water-soluble hydroxycamptothecin sodium salt (HCPT-Na) was incorporated into these vesicles during the osmotic treatment, forming RBC@HCPT. These vesicles were then downsized to approximately 120 nm via physical extrusion. Crucially, an acidification-induced crystallization method was employed, using the sealed vesicles as microreactors to convert the encapsulated HCPT-Na into nanocrystals, ultimately yielding the nRBC@HCPT platform.

The resulting nRBC@HCPT inherited the "stealth" properties of RBCs, evading immune clearance to achieve prolonged blood circulation and enhanced tumor accumulation. It demonstrated markedly superior antitumor efficacy over commercial hydroxycamptothecin injections across diverse models, including mouse breast cancer, orthotopic liver cancer, and patient-derived xenograft (PDX) models. Furthermore, nRBC@HCPT induced immunogenic cell death, and its combination with an anti-PD-1 antibody synergistically enhanced antitumor immunity, significantly prolonging survival in mice. For clinical translation, the system can be prepared from RBCs of all blood types (A, B, AB, O) for matched transfusions. The excellent redispersibility and stability of its lyophilized powder facilitate long-term storage, underscoring its strong potential for commercial development as a next-generation therapeutic platform.

Selenized neural stem cell-derived exosomes: a neotype therapeutic agent for traumatic injuries of the central nervous system

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Traumatic injuries to the central nervous system (CNS), including traumatic brain injury (TBI) and spinal cord injury (SCI), often have devastating consequences and are the leading causes of long-term disability across all age groups [1]. Oxidative damage and neuroinflammation are the hallmarks of exacerbated traumatic injury to the central nervous system (CNS). Drawing inspiration from the neuroprotective properties of exosomes derived from neural stem cells (NExo) and the reactive oxygen species (ROS) scavenging capacity of selenium, we developed an advanced NExo bearing ultrasmall nano-selenium (~3.5 nm) via lipid-mediated nucleation (SeNExo). In addition to maintaining the biological components of NExo, the resulting SeNExo exhibited a unique Se-O bond that dramatically enhanced its ROS scavenging performance. We elucidated that SeNExo utilized ligand (APOE)_receptor (LRP-1) interactions for blood-brain barrier (BBB) penetration. Through extensive analysis of proteomics, miRNA omics, and single-nucleus RNA sequencing, we revealed that SeNExo could alleviate neuronal apoptosis, restore glia homeostasis, and remodel glia-neuron network. Therefore, SeNExo conferred potent therapeutic benefits, significantly reducing cerebral lesions in a murine traumatic brain injury model. Even extending to a murine spinal cord injury model, we also observed the effective promotion of locomotory recovery, further support SeNExo as a neotype and a promising therapeutic agent for treating traumatic CNS injury.

Keywords: Neural stem cells, exosomes, selenium, blood-brain barrier, CNS injury

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A live biohybrid bacterial therapy based on engineered Serratia marcescens

Abstract

Bacteria-inspired therapeutic systems are emerging as promising translational biomaterials due to their inherent tumor-targeting capabilities and engineering versatility. However, clinical translation remains limited by the lack of safe microbial chassis and complex material modifications. Here, we present a biosynthetic, biohybrid Serratia marcescens platform engineered for anticancer therapy. The attenuated strain was designed to overproduce the photosensitive pigment prodigiosin through intrinsic biosynthetic pathways, forming a self-contained therapeutic entity.

The engineered S. marcescens exhibited a bright red phenotype, potent cytotoxicity ($IC_{50} < 4\times10^7$ CFU/mL, equivalent to 0.5 μmol prodigiosin), and near-infrared responsiveness, enabling photo-controllable activation and in vivo bacterial clearance within three minutes. In murine B16F10 and CT26 tumor models, the biohybrid platform elicited robust immune activation, including dendritic cell maturation, T-cell infiltration, and macrophage polarization toward an antitumor phenotype.

This study demonstrates a fully biosynthetic and controllable microbial platform that bridges synthetic biology and biomaterials for translational cancer therapy, offering a safe and adaptable strategy for future clinical development.

BIFUNCTIONAL ULTRASOUND-CONTROLLABLE β-GLY NANOPATCH FOR TBI REPARI

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Traumatic Brain Injury (TBI) is the leading cause of disability and death among young and middle-aged adults worldwide, with no effective clinical therapies currently available. Neural Stem Cell (NSC)-based therapy brings great hope for TBI repair, but issues such as low in vivo neural differentiation efficiency and poor NSC survival caused by the hostile neuroinflammatory microenvironment limit its application. Electrical stimulation is regarded as an effective measure for regulating the neural differentiation of NSCs; however, problems including the non-degradability of traditional piezoelectric materials and the limited efficacy of single-target interventions severely hinder its translational efficacy. To address these bottlenecks, we innovatively designed an ultrasound-controllable, bifunctional, and degradable piezoelectric nanopatch, using β-glycine (β-Gly) as the core piezoelectric component, which possesses both ultrahigh piezoelectric coefficients and excellent biocompatibility as a natural amino acid. We resolved the inherent phase transition and rapid dissolution issues of β-Gly through the nano-confinement effect and PLGA encapsulation technology, meanwhile, we integrated anti-inflammatory drugs into the encapsulation layer and modified it with laminin, enabling the stable anchoring and dynamic tracking of NSCs.

After injectable delivery, the nanopatch can migrate alongside neural stem cells (NSCs); under ultrasonic mediation, it achieves synchronized targeted controlled release of anti-inflammatory drugs under ultrasonic mediation, effectively inhibiting acute neuroinflammation and increasing the survival rate of NSCs to over 85%; meanwhile, it can realize wireless non-invasive electrical stimulation, significantly promoting the differentiation of NSCs into neurons with the neuronal proportion reaching 45%. The material possesses in vivo degradable properties, which can avoid long-term toxicity and invasive tissue damage, and its minimally invasive administration route fully meets the needs of clinical applications. This interdisciplinary design provides a novel paradigm for TBI treatment, significantly enhancing the translational potential of NSC therapy and holding substantial application value for the repair of clinically refractory traumatic brain injury.

Nanomaterial-Genetics Enables Receptor-Guided Targeting of Ligand-Functionalized Nanoparticles for Cell-Type–Specific Neuromodulation

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Abstract

Stimuli-responsive nanomaterials have emerged as powerful tools for neuromodulation, yet their lack of cell-type specificity remains a major barrier to their broader application. Here, we introduce *nanomaterial-genetics*, a hybrid strategy that integrates genetically encoded synthetic receptors with ligand-functionalized nanoparticles to achieve receptor-guided and cell-selective targeting. In this system, cells or neurons are engineered to express a designed receptor that selectively recognizes and binds a complementary ligand displayed on the nanoparticle surface. Using this principle, we functionalized gold nanoparticles with tailored ligands (AuNP–ligands) and demonstrated that receptor-expressing cells or neurons exhibit robust and selective photothermal responses to near infrared irradiation at ultralow nanoparticle concentrations, whereas non-expressing cells remain largely unresponsive. This low-dose requirement substantially reduces nanomaterial-associated cytotoxicity. The receptor–ligand nano-interface thus offers a versatile platform for directing nanomaterials to genetically defined cell types, enabling cell-type–specific delivery of AuNP–ligands and precise optothermal neuromodulation capable of modulating mouse behaviors. Together, these results establish nanomaterial-genetics as a generalizable conceptual framework that bridges genetic engineering and nanomaterial design. Beyond providing a minimally invasive and highly specific neuromodulation toolkit, this strategy opens broad opportunities for applications requiring cell-specific nanoparticle targeting.

Formulation-Driven Brain Targeting: Mechanistic Insights and Therapeutic Applications

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Efficient brain delivery of therapeutics remains a major challenge due to the restrictive nature of the blood–brain barrier. Intranasal (IN) administration provides a non-invasive route to bypass this barrier, yet the formulation parameters governing optimal nose-to-brain transport are still not fully elucidated. In this study, we investigated how nanocarrier microstructure and mucin interactions influence CNS delivery efficiency. Two formulation platforms were examined: (i) poloxamer-based nanogels containing surfactant variants A, B, or C2, and (ii) liposomal carriers with modulated C-content (11CND) designed to adjust membrane rigidity. The nanogels exhibited particle sizes of 94.3 ± 1.1 to 132.9 ± 3.6 nm, with C2-based systems demonstrating the loosest internal structure and the highest drug release rate in a mucin-rich environment. Both A- and C2-formulations displayed mucin-interaction strengths at least 20-fold greater than poloxamer alone ($\Delta G'$), enhancing nasal cavity retention and enabling prolonged diffusion toward the olfactory bulb. Similarly, the 11CND liposome showed a 4.3-fold increase in brain accumulation versus its native counterpart, attributed to optimized rigidity and viscoelastic balance that maintained structural stability while promoting shear-responsive mobility during nasal airflow.

Therapeutic evaluation of Urocortin-loaded 11CND in a rat intracerebral hemorrhage (ICH) model demonstrated a 30% reduction in hemorrhagic lesion volume and a >35% improvement in neurological function within three days following IN administration. Together, these findings reveal that controlled modulation of carrier structure and mucin-interaction strength governs nasal retention, release dynamics, and neuronal pathway transport. This formulation-driven strategy offers a rational design framework for non-invasive, brain-targeted therapies in CNS diseases.

Nanozymes expanding the boundaries of biocatalysis

Biocatalysis lies at the core of life processes and sustainable development. With the discovery of protein enzymes, ribozymes, and the development of artificial enzymes, the scope of biocatalytic systems has continuously expanded. The emergence of nanozymes has further extended the boundaries of biocatalysis. Characterized by abundant active sites, multiphase catalytic features, and exceptional structural stability, nanozymes exhibit unique physicochemical properties that overcome the limitations of natural enzymes in substrate scope, environmental adaptability, and application scenarios. These advantages have driven innovative applications of biocatalysis in medicine, agriculture, environmental protection, and industry. Moreover, several natural nanostructures (e.g., magnetosomes and ferritin cores) have been found to possess intrinsic catalytic activity, suggesting that natural nanozymes may play essential roles in physiological regulation and the origin of life.

The speaker has conducted a series of systematic studies on nanozymes as a novel biocatalytic system: (1) elucidated the structure–activity relationships of nanozymes and established new de novo design strategies for creating high-performance nanozymes with catalytic activities surpassing those of natural enzymes; (2) discovered natural nanozymes with intrinsic antioxidative physiological functions, and unveiled their catalytic mechanisms as well as evolutionary patterns across species; (3) developed novel antioxidative nanozyme-based catalytic therapeutic strategies, which have shown promising preclinical potential in disease models such as stroke and Parkinson’s disease; and (4) pioneered low-temperature catalytic nanozyme technologies, offering new approaches to biomass degradation and other applications in cold environments.

Biomimetic nanozymes for hard-to-treat inflammatory disease therapy

Nanozymes are biomimetic functional nanomaterials. Due to their superiority to enzymes and conventional artificial enzymes in terms of stability, enduring catalysis, and multifunctionality, nanozyme have shown promise in treating various diseases including inflammatory diseases. Such efficacy is generally achieved via the antioxidation and anti-inflammation activity. Nevertheless, chronic inflammation-induced diseases including cancer are still very challenging. To address this challenge, by analyzing clinical samples, we are able to identify key chemokines involved in the chronic inflammation-induced diseases. We further engineer the nanozymes together with the chemokines. The obtained biomimetic nanozymes exhibit better efficacy than small molecular medication and antibodies, demonstrating the promise of nanozymes for hard-to-treat inflammatory disease therapy.

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FABRICATION OF PROGRAMMABLE MULTISCALE HYDROGELS WITH SUB-MICROMETER PRECISION FOR ENGINEERED TISSUES

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Millions of soft tissue injuries occur annually, while current biomaterial scaffolds often result in fibrotic rather than regenerative healing. While the incorporation of cells, peptides, or growth factors can enhance regeneration, these strategies face translational barriers due to high cost and safety concerns. Decellularized extracellular matrices also remain limited by immune rejection risks and inconsistent sourcing. Conventional hydrogel scaffolds are further hindered by mismatched degradation kinetics. Rapid degradation causes loss of mechanical support, while slow degradation restricts cell infiltration and tissue formation. Granular hydrogels composed of hydrogel microparticles provide inherent microporosity and injectability, but their non-porous particles limit pore connectivity and volume, often leading to incomplete tissue integration and fibrosis. To overcome these limitations, we developed porous particle-based granular (PPG) hydrogels, with highly interconnected internal porosity to promote soft tissue regeneration. Using a controlled liquid–liquid phase separation method, we fabricated hydrogel particles containing continuous internal pores that enhance total pore volume, interconnectivity, and surface area. This architecture enables efficient cell infiltration, balanced scaffold degradation, and enhanced tissue organization. In murine and porcine wound models, PPG hydrogels significantly facilitates mature vascular network boosts pro-regenerative macrophage polarization (M2/M1) and CD4+/Foxp3+ regulatory T cells, culminating in scarless skin regeneration enriched with hair follicles. Moreover, our hydrogels outperform the clinical gold-standard collagen/proteoglycan scaffolds in a porcine model, showcasing superior cell infiltration, epidermal integration, and dermal regeneration. Importantly, these regenerative outcomes were achieved without exogenous cells or biologics, demonstrating strong potential for safe, cost-effective clinical translation in tissue regeneration.

Robust Protein-Engineered Porous Architectures for Biomimetic Alveolar Tissue and Lung-on-a-Chip Platforms

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The precise fabrication of protein-based biomaterials that mimic the porous and elastic architecture of alveolar tissues remains a major challenge due to the difficulty of simultaneously controlling microstructural porosity and mechanical properties. In this study, we developed a fabrication strategy that utilizes the *macromolecular crowding effect* to induce the self-assembly of peptide-based materials, combined with a *foaming platform* capable of finely tuning porosity and pore size. This approach enabled the creation of highly elastic, porous protein scaffolds that closely replicate the structural scale and mechanical compliance of native alveoli. The fabricated structures exhibited tunable porosity, pore size, and mechanical strength depending on the process parameters, including pneumatic pressure, foaming agent concentration, bioink composition, and temperature. Optimization of these parameters yielded scaffolds with high stability and biocompatibility. Under *in vitro* conditions, cyclic stretching and relaxation stimuli were applied to mimic breathing motion, promoting the differentiation of alveolar epithelial cells and the formation of air–blood barrier–like architectures. The proposed fabrication strategy for high-elasticity, porous protein scaffolds offers a simple yet powerful platform for engineering tissue-specific microenvironments. Furthermore, the incorporation of bioactive molecules and extracellular matrix components enables its extension to other tissue models, such as lung, bone, and liver, and provides a versatile approach for developing multi-organ-on-chip systems and regenerative medicine applications.

Acknowledgements

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Submission Title:

Engineering an ex vivo pancreas–myosteatosis muscle tissue via biofabrication

Learning Objective:

Submission Details:

Interactions between pancreatic cells and skeletal muscle play essential roles in regulating systemic metabolic homeostasis. In this study, we developed an ex vivo dual-tissue platform that reconstructs pancreas-specific microenvironments alongside a myosteatosis-mimetic muscle construct using complementary biofabrication approaches. A tissue-specific hydrogel derived from bovine pancreas decellularized extracellular matrix (pdECM) was employed to promote the rapid formation of uniform INS-1 cell spheroids via a photo-crosslinkable surface-coating method. These pancreatic constructs exhibited preserved ECM compositions and stable secretion profiles while maintaining key β-cell properties. In parallel, an electric field–assisted bioprinting process was used to fabricate aligned myofiber structures that reflect the anisotropic architecture of native skeletal muscle. To emulate fat infiltration observed in myosteatosis, differentiated 3T3-L1 adipocytes were integrated within the printed muscle fibers, forming a composite tissue that exhibits both myogenic and adipogenic features. Gene expression and immunofluorescence analyses confirmed the coexistence and spatial organization of these lineages within the engineered construct. By combining pancreas-derived biochemical cues with structurally aligned muscle fibers and adipocyte incorporation, this biofabricated dual-tissue platform provides a controllable and physiologically relevant system for studying inter-tissue metabolic communication. The proposed approach establishes a reproducible foundation for exploring complex pancreas–muscle interactions and evaluating tissue-level responses under various metabolic or structural perturbations.

Submission Title:

Mushroom Chitosan–Collagen Bioink and Comb-Integrated Bioprinting for Bone–Tendon Interface Regeneration

Learning Objective:

This presentation will explain how mushroom-derived chitosan–collagen bioink and comb-integrated shear-alignment bioprinting work together to improve collagen organization, cell behavior, and scaffold performance, offering a promising strategy for bone–tendon interface regeneration.

Submission Details:

We developed a novel collagen-based bioink incorporating mushroom-derived chitosan extracted and characterized from Pleurotus ostreatus. This biomaterial offers a safe and sustainable alternative to crustacean-derived chitosan, overcoming limitations such as allergenicity and ethical concerns. The mushroom chitosan-collagen bioink demonstrated excellent biocompatibility, antibacterial activity, and immunomodulatory effects. When used to fabricate 3D-printed scaffolds composed of mushroom chitosan, hydroxyapatite, and collagen, human adipose-derived stem cells (hASCs) exhibited enhanced adhesion, proliferation, and differentiation, along with reduced inflammatory cytokine expression compared to collagen-only controls. To address the challenge of replicating the micro-architectural organization of native tissues, we additionally introduced a comb-integrated nozzle bioprinting technique. This system applies controlled shear stress during printing to align collagen fibrils, thereby generating defined topographical cues that promote cell alignment. The printing parameters, including temperature, nozzle speed, and bioink flow rate, were systematically optimized. Live/Dead assays confirmed high cell viability (~90%), and morphological and gene expression analyses demonstrated improved cellular alignment and tissue-specific responses relative to conventional bioprinting methods. Collectively, the synergy between the bioactive mushroom chitosan-collagen bioink and the shear stress-induced collagen alignment achieved through comb-integrated 3D bioprinting establishes a promising platform for bone-tendon interface regeneration, offering enhanced structural fidelity and superior biological performance.

EXTRACELLULAR MATRIX-REGULATED MICROGLIAL MIGRATION AND NEURON SELF-ORGANIZATION

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The brain's functional integrity depends on the coordinated behavior of its resident immune cells and neurons, both of which are exquisitely sensitive to mechanical cues within the extracellular matrix (ECM). In this series of studies we dissect how mechanical signals regulate microglial migration and neuronal self-organization. Using acute brain-slice cultures and employing an actuator fabricated from a magnetically driven soft material to deliver precisely calibrated tensile strains, we show that microglia exhibit rapid, directed migration toward remote tensile fields transmitted through the ECM, and further identify by pharmacological and genetic perturbations that the mechanosensitive ion channel Piezo1 is a pivotal mediator of this response. In parallel, we demonstrate that three-dimensional ECM constructs with defined composition and viscoelastic properties guide primary neurons into distinct architectural phenotypes—dynamic chains, stable networks, or compact clusters. Multimodal analyses (e.g., label-free traction-force microscopy, Western blot, and siRNA knock-down) reveal that ECM-driven mechanochemical coupling modulates cytoskeletal tension, adhesion-molecule expression, and reciprocal force generation, and thereby dictates emergent neuronal patterning.

VISCOELASTIC SILK CRYOGELS FOR BONE TISSUE REGENERATION

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The viscoelastic properties of biomaterials with tunable stress relaxation behaviors positively influence stem cell responses and promote tissue repair. In this study, we developed silk fibroin-based macroporous viscoelastic cryogels with rapid stress relaxa-tion behaviors for repairing critical-size skull defects. Freezing crosslinking and water annealing treatments were employed to modulate the stress relaxation behavior. Fourier transform infra-red (FTIR) spectroscopy revealed that the cryogels primarily consists of 30% stable Silk I structure with a type II β-turn conformation and exhibits rapid stress relaxation behavior. Prolonging the freeze cross-linking duration and exposing the cryogels to 65 °C water vapor promotes the transformation of random coils and α-helices into β-sheets and turns and bends, thereby slowing the stress relaxation rate and enhancing the material elasticity. In vitro macrophage culture experiments demonstrated that cryogels with rapid stress relaxation promote macrophage polarization toward the M2 phenotype, significantly reduce the expression of pro-inflammatory cytokines such as IL-6, and enhance the expression of pro-regenerative cytokines such as IL-10. Results from a rat critical-size skull defect model demonstrated that, compared to elastic cryogels, viscoelastic cryogels accelerated defect repair. Single-cell RNA sequencing further revealed that viscoelastic cryogels significantly enhanced macrophage infiltration and increased the proportion of $CD163^{+}$ macrophages. This study is expected to provide new theoretical insights for the biomechanical and structural design of clinical bone repair materials.

Key words: Silk fibroin; Viscoelasticity; Stress relaxation; β-turn; Skull repair

Janus Silk-based Patch with Temporary Adhesion for Inflammatory Mediators Removal in Corneal Alkali Burn Treatment

Corneal alkali burns cause persistent inflammation, leading to corneal vascularization and fibrosis, which severely impair vision. Here, we developed a temporary adhesive and detachable Janus silk-based patch to capture and remove inflammatory mediators from the ocular surface. The lower silk layer of the Janus patch incorporates of polyamidoamine and heparin, offering adsorption capacity for inflammatory mediators on the ocular surface. The upper hyaluronan layer imparts lubrication, alleviating foreign-body sensation and reducing shear stress from blinking. The integration of the silk and hyaluronan layers is achieved through interfacial diffusion, liquid–liquid phase separation, and photopolymerization, resulting in a stable interpenetrating network interface. After water annealing, the Janus patch exhibited excellent transparency, mechanical strength, and swelling resistance, remaining attached to the rat ocular surface for 3–5 days. Adsorption tests confirmed that the patch effectively captured small-molecule dyes, proteins, and free DNA. In the rat corneal alkali burn model, imaging and histological evaluations showed significant reductions in vascularization and fibrosis after 3 days of treatment, along with improved corneal transparency. RNA sequencing revealed that patch treatment effectively inhibited the PI3K–AKT inflammatory pathway. This inflammation-removing patch represents an innovative treatment for corneal alkali burns with significant clinical potential.

SILK-BASED MULTILAYER COATINGS FOR ANTICOAGULATION AND DURABILITY IMPROVEMENT IN ECMO HOLLOW FIBER MEMBRANES

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Abstract: In clinical extracorporeal membrane oxygenation (ECMO), prolonged blood residence time in oxygenators can lead to thrombus formation and complications. Heparin-based bioactive coatings are commonly used for anticoagulation, but prolonged shear stress during blood flow can cause heparin desorption, degradation, and inactivation, reducing durability and antithrombotic efficacy. In this study, we developed a silk fibroin (SF)-based multilayer coating to enhance both mechanical stability and anticoagulant performance. A SF foundation layer was first fabricated on hollow-fiber membranes using layer-by-layer (LbL) self-assembly. Then SF acted as a bridge to assemble heparin and albumin through electrostatic interactions, followed by crosslinking to stabilize the structure, resulting in a uniform SF-heparin-albumin composite coating with controllable thickness. 10-day shear oscillation and nanoscratch tests showed that the SF bridging layer significantly improved mechanical robustness and interfacial adhesion. In vitro and in vivo blood circulation assays demonstrated hemocompatibility, with reduced platelet adhesion, prolonged coagulation time, and enhanced antithrombotic performance. Blood-gas exchange tests using a miniaturized oxygenator confirmed that the coating did not impair gas transfer efficiency. In summary, the SF bridging layer effectively links the substrate to bioactive components, improving long-term mechanical integrity and anticoagulant properties without compromising oxygenator function.

SEMICONDUCTOR BIOMATERIALS FOR TISSUE REGENERATION

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In biological systems, life processes can be viewed as highly regulated by bioelectrical signaling through semiconductor-like mechanisms—ion channels in cell membranes exhibit field-effect transistor characteristics, while collagen fibers in the extracellular matrix display mechanoelectrical responsiveness. Together, these semiconductor-like components orchestrate bioelectrical activities essential to life. Emulating such biological traits in synthetic semiconductors offers a promising strategy to address the long-standing challenge of tissue repair at the interface of implantable materials.

Inspired by the heterogeneous electrical microenvironment within the nanodomains of bone collagen fibrils, our team developed a semiconductor-based nanofibrous heterojunction coating via nanoscale in situ nucleation, enabling the controllable formation of built-in electric fields at the nanoscale, mimicking the native electrical microenvironment of bone. We found that the nanoscale electric fields polarize macrophages toward a M2 pro-angiogenic phenotype, enhancing secretion of angiogenic factors and accelerating bone integration at the implant interface. Furthermore, we engineered microscale built-in electric fields on ferroelectric implant surfaces through selective phase transition induced by localized polarization. Cells cultured on these substrates elongated perpendicular to the electric field lines, with intracellular calcium ions accumulating at the leading edge in low-potential regions, forming a polarization gradient exceeding threefold. This intracellular Ca^{2+} gradient, driven by the material's built-in electric field, generates an endogenous cellular electric field that promotes angiogenesis through a mechanoelectrical feedback loop. Looking forward, semiconductor-based biomaterials, with their self-generated and field-responsive electrical properties, are poised to open new avenues for controlling tissue regeneration.

Acknowledgement

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SILICATE BIOMATERIALS‐INDUCED BONE MARROW ORGANOIDS FOR TISSUE REGENERATION

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The bone marrow is essential for immune function, hematopoiesis, and skeletal system. The emergence of bone marrow organoids (BMOs) holds promise for addressing bone‐related deficiencies, although maintaining BMOs homeostasis is still challenging, and their efficacy for tissue regeneration remains uncertain. Silicate biomaterials can provide distinctive biochemical clues by releasing bioactive ions, which are beneficial for regulating stem cell behaviors and developing cell functions. In this study, harnessing the bioactivities of silicate biomaterials, we engineered functional BMOs through the culture of mesenchymal stem cells (MSCs) and endothelial cells in a chemically defined medium, incorporating with calcium silicate nanowires (CS) and magnesium silicate nanospheres (MSS). The resulting BMOs demonstrated robust preservation of endothelial networks, increased self‐renewal of the mesenchymal compartment, and positive effects on hematopoietic stem cells. Co‐culture experiments revealed that the engineered BMOs can significantly improve the activities of chondrocytes, MSCs, and Schwann cells, which are pivotal for tissue regeneration. Furthermore, the silicate biomaterials upregulated gene expression and signaling pathways in the domains of osteogenesis and angiogenesis. In a rabbit osteochondral repair model, BMOs induced by MSS notably enhanced osteochondral regeneration. Our study reveals the critical role of silicate biomaterials in augmenting BMOs homeostasis and function, providing an innovative and compelling strategy for future tissue regeneration.

Title：3D Printing of Biomimetic Biomaterials and Transformation

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Abstract：
3D printing technology is one of the most promising technologies in the fields of tissue engineering and regenerative medicine, which can stack multiple components (materials, cells, etc.) layer by layer in three-dimensional space to construct complex and accurate structures. Therefore, for the construction of tissue regeneration scaffolds, 3D printing methods have far surpassed other traditional manufacturing methods. How to construct personalized tissue regeneration scaffolds with different compositions, structures, and functions through smart design and 3D printing technology is a research focus in the field of regenerative medicine. We have conducted a series of research work to meet the needs of biomimetic and functional 3D printing scaffolds, from material design, structural regulation, functional modification, and multi cell printing of artificial tissues. We have developed various 3D printing tissue regeneration scaffolds with excellent biological functions. Firstly, we prepared a series of biomimetic scaffolds with excellent tissue repair performance by regulating the macro/micro structure of 3D printed scaffolds. Macroscopically, through precise model design, printing out scaffolds with biomimetic lotus root and natural bone multi-level structures can effectively promote vascularized bone regeneration. At the micro level, by combining microbial catalysis and other technologies with 3D printing technology, a 3D printed scaffold with a specific micro nano structure is constructed, significantly improving the osteogenic performance of the scaffold. For tissue defects caused by diseases, scaffolds with a single repair function cannot achieve the ideal treatment goals. Therefore, we further combined 3D printing technology with surface modification strategies to develop various 3D printing scaffolds with dual functions of tumor treatment and tissue regeneration, thereby more efficiently curing defects caused by tumor diseases. In addition, for the regeneration and construction of complex tissues/organs, it is necessary to develop biomimetic scaffolds with a regular arrangement of multiple cells. Therefore, we further extend 3D material printing to 3D multicellular printing, by regulating the composition of inorganic bioinks, designing cell spatial distribution, and constructing multicellular scaffolds that simulate different complex tissues. The multicellular scaffold constructed through 3D cell printing has excellent tissue regeneration function both in vivo and in vitro, which offers a foundation for the three-dimensional reconstruction of other complex tissues/organs.

Enhanced Cardioprotection via Modulation of Epithelial–Mesenchymal Transition by Cell-Clustering Biosynthetic Phages

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Abstract

Cardiac repair following myocardial infarction (MI) remains limited, as conventional therapies focus on preventing further damage rather than promoting true cardiac regeneration. Inducing a controlled epithelial–mesenchymal transition (EMT) within the epicardium has recently emerged as a key regenerative mechanism, enabling epicardial-derived cells to contribute to neovascularization and tissue remodeling. Here, we report a biosynthetic phage–mesenchymal stem cell (MSC) cluster patch that harnesses mechanobiological signaling to drive epicardial EMT and enhance cardioprotection. The engineered filamentous phage, genetically programmed to display high-density integrin-binding motifs on its pVIII coat protein, promotes high-avidity clustering with MSCs and elicits robust focal-adhesion formation. This clustered architecture activates YAP/TAZ signaling, initiating paracrine reprogramming and EMT induction in the epicardial layer. When applied as a patch onto a rat cardiac ischemia–reperfusion injury (IRI) model, the Phage–MSC Cluster system markedly reduced infarct size, preserved ventricular function, and stimulated neovascular and stromal regeneration without systemic toxicity. Transcriptomic profiling of the regenerated myocardium revealed suppression of fibrotic signaling and upregulation of genes associated with angiogenesis, oxidative-stress resilience, and epicardial EMT activation. Collectively, these findings establish cell-clustering biosynthetic phages as programmable mechanobiological materials that couple

high-avidity cell adhesion with precise EMT modulation, offering a new paradigm for epicardium-driven cardiac regeneration and functional cardioprotection.

Keywords

Cardiac regeneration; Epithelial–mesenchymal transition (EMT); Biosynthetic phage; Myocardial infraction (MI), ischemia-reperfusion injury

Stimuli-Responsive Nanopattern Platforms for Autonomous Stem Cell Differentiation

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During early development, stem cells respond to temporally orchestrated biochemical signals that guide lineage specification. Reproducing such time-regulated cues in vitro remains a major challenge, as conventional differentiation protocols rely on repetitive factor supplementation and manual timing control. In this study, we propose a hybrid nanopattern system capable of autonomously inducing neural differentiation from pluripotent stem cells through external stimulus–responsive release of instructive molecules. The platform integrates nanostructured arrays with functional nanoparticles that provide spatially confined and temporally tunable biochemical environments. Upon external stimulation, local microenvironments are dynamically modulated, leading to sequential activation of signalling pathways associated with neurogenesis. This spatiotemporal control enables highly reproducible differentiation without repeated media exchanges or additional supplements. The resulting neural stem-like cells exhibit uniform morphology and characteristic lineage markers, demonstrating the feasibility of autonomous, on-demand differentiation. Overall, this approach simplifies cell-culture workflows and provides a versatile tool for studying neural development and constructing organoid-based models.

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Keywords: Stem cell differentiation, Neural induction, Hybrid nanomaterials, and nanopatterning

FULL ORGAN MANUFACTURE: PARALLEL COAXIAL PRINTING FOR MULTISCALAR CIRCULATION SYSTEM

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Large-scale organ manufacture has been recognized as a promising solution for organ transplantation resulting from organ failure. Due to its ability to manipulate multiple components, direct-ink-writing (DIW) bioprinting has become widely adopted in the field. However, challenges such as the long-time process of channel switching and the low efficiency in fabricating tubular structures have hindered the goal of constructing complex tissues with diverse cell types and hierarchically interconnected vascular networks. Here, we introduce a biomanufacturing approach called multi-nozzle aided parallel co-axial additive manufacture (MAPCAM). In this approach, we designed: 1) an engineered granular bioink, characterized by its self-supporting, shear-thinning, and self-healing properties; and 2) a core-protruding co-axial nozzle, modifying the traditional co-axial nozzle by elongating the core nozzle. During the printing, the core nozzle could lacerate the shell and connect the core-ink when the co-axial nozzle moves across a printed filament. The shear-thinning characteristics of the granular bioink facilitate easy piercing or scratching of the shell by the core nozzle, allowing for efficient replacement with new shell bioink. With the help of supporting filaments constructed by multi-nozzles, the tubular structure printed by a core-protruding co-axial nozzle could be supported in all directions. In addition, owing to the good biocompatibility of the granular bioink, cells can be embedded within the shell of the tubular structure. This methodology enables the in vitro reconstruction of multi-component, complex tissues with interconnected networks; for example, it becomes feasible to bioprint a full-size kidney.

STUDY ON TISSUE REPAIR BIOMATERIALS ADAPTED TO PATHOLOGICAL MICROENVIRONMENT

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Abstract

In the process of tissue repair, due to different diseases, the pathological microenvironment is very complicated and the repair process is difficult to control. Focusing on the key scientific issues of how to adapt the complex pathological microenvironment and achieve the controllability of tissue repair, our research group has developed a series of multi-functional tissue repair materials. On the one hand, for hard tissue bone diseases, functional elements such as peptides and cell membranes that can target the bone pathologic microenvironment are designed for biomimetic modification of materials, realizing efficient treatment of bone infection, osteosarcoma, bone defects and other diseases. On the other hand, for soft tissue wounds, functional gel, double-layer microneedles and other material systems were constructed, which effectively solved the problems of long inflammatory cycle and angiogenesis disorders. In addition, "wound repair dressing" (Class II medical device, approved) and "Wound repair microneedle" (Class III medical device, pilot stage) were developed based on gel/microneedle materials.

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Nanoparticle Mediated Dox-iron Target Therapy Wiping out Malignant Stem Cells in Blood Cancer

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Acute myeloid leukaemia (AML) is an aggressive blood cancer marked by the uncontrolled growth of immature myeloid cells in the bone marrow. It is the most common acute leukaemia in adults, accounting for about 1% of all cancers worldwide. Despite current treatments, the five-year survival rate remains below 30%, largely due to relapse driven by therapy-resistant leukaemia stem cells (LSCs). Conventional therapies, including chemotherapy and stem cell transplantation, often fail to eliminate LSCs, underscoring the need for novel, targeted strategies to overcome resistance and prevent relapse.

To address this challenge, we developed a novel micellar nanoparticle that integrates advances in nanotechnology and molecular oncology for the targeted delivery of chemotherapeutic agents to leukemia cells and LSCs. The micelle is synthesized from a multifunctional copolymer featuring a hydrophobic core containing crosslinking and fluorophore blocks and a hydrophilic shell comprised of ligand-anchorable Maleimide and antibiofouling blocks, providing exceptional stability and resistance to protein adsorption under physiological conditions. It achieves an encapsulation efficiency exceeding 70% for the doxorubicin–iron complex, with minimal drug leakage (<20% within 24 hours), and includes fluorescent functionality to enable real-time biodistribution tracking. For selective targeting, we have used Maleimide-thiol interactions to functionalize the surface of micelles with RSPO3 ligands that bind specifically to the LGR4 receptor, which is overexpressed on the surface of LSCs. This design enables precise drug delivery and enhanced therapeutic specificity while minimizing off-target toxicity. In vitro studies have confirmed its biocompatibility, targeted uptake, controlled drug release, minimal protein adsorption, and almost no hemolysis, while ongoing in vivo studies in mice are evaluating its biodistribution and therapeutic efficacy in treating AML.

Fibronectin-guided immune-stromal cell crosstalk promotes angiogenesis in pulp-dentin complex regeneration

Macrophages are multifunctional immune cells that play crucial roles in immune regulation and tissue regeneration through interactions with various cell types. Although macrophage-stromal cell interactions are widely recognized as essential for tissue regeneration and homeostasis, their precise mechanisms in the pulp-dentin complex, a key functional unit for tooth maintenance, remain incompletely understood. Here, we investigated macrophage interactions with dental pulp stromal cells (DPSCs) in the dental pulp microenvironment in response to the infection caused by dental caries. As caries progressed, macrophage-DPSC interactions became increasingly prominent. Whole-transcriptome analysis revealed that these interactions are mediated by fibronectin-integrin engagement, which induces a phenotypic shift in macrophages from pro-inflammatory to pro-angiogenic, mediated by upregulation of angiogenic chemokines. Integrated analysis of a single-cell RNA sequencing dataset from human pulp tissue further confirmed that caries progression enhances macrophage-driven angiogenic signaling toward the endothelial cell population. Moreover, the altered secretome resulting from macrophage-DPSC co-culture significantly enhanced in vitro endothelial tube formation and survival, indicating a strong angiogenic potential conducive to tissue regeneration. In a preclinical pulp revascularization model, pre-injection of fibronectin solution into the pulp cavity promoted robust neovascularization and resulted in dentin-pulp complex regeneration and complete root development including apical closure. Collectively, these findings identify fibronectin as a key regulator that reprograms the damaged pulp environment into a pro-angiogenic and regenerative niche through coordinated immune-stromal interactions. This study offers a promising direction for developing extracellular matrix-based therapeutic strategies in regenerative dentistry.

Crowding as a design lever: Tuning Collagen (I) Fibrillogenesis and Bioactivity via Crowder Library

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Collagen (I) undergoes spontaneous fibrillogenesis and sol-gel transition under physiological pH and temperature. However, the prolonged timescale of this process limits its clinical application. Inspired by the superior efficiency of biochemical processes in vivo milieu compared with dilute in vitro conditions, we screened and characterized diverse crowders to accelerate collagen (I) assembly. Our study establish crowding-accelerated collagen assembly as a general principle across across various kinds of crowders, from which we compiled a comprehensive crowder library. Systematic analysis of key parameters governing the crowding effect enabled flexible control over gelation timescales. Moreover, we introduce, for the first time, a dual-benefit strategy that selects bioactive crowders according to specific regenerative needs, thereby achieving rapid gelation while endowing collagen gels with on-demand bioactivities. In a myocardial infarction application, , collagen gel formulated with pro-angiogenic and anti-fibrotic crowders served as a stem cell carrier and yielded marked improvements in cardiac repair. This straightforward and versatile strategy considerably expands the materiobiology toolkit and inspires the design and applications of innovative collagen (I)-based materials.

Research on Three-Dimensional Porous Scaffold Materials with Mechano-Electrical Response

Objective: Based on the biomechanical principle that bone tissue can generate intrinsic bioelectrical signals under stress stimulation, this study aims to design and fabricate a three-dimensional porous scaffold with mechano-electrical response characteristics, in order to mimic the natural physiological microenvironment of bone. This work provides a theoretical basis and technical pathway for the development of new-generation smart bone repair materials.

Methods: A near-field electrospinning writing technique was employed to fabricate a highly ordered and aligned three-dimensional porous scaffold using the piezoelectric polymer material P(VDF-TrFE). The scaffold was characterized using scanning electron microscopy (SEM) and other methods for its material properties, and its biological performance was evaluated through in vitro cell co-culture experiments.

Results: SEM characterization confirmed the successful construction of a well-defined three-dimensional hierarchical pore structure within the scaffold, incorporating both macro-pores and micro-pores. Results from the 14-day cell co-culture Live/Dead staining demonstrated a high density of live cells with well-spread morphology on the scaffold surface, along with sparse and scattered dead cells. This fully substantiates the excellent cytocompatibility of the developed mechano-electrically responsive 3D porous scaffold.

Conclusion: This study confirms that the designed mechano-electrically responsive three-dimensional porous scaffold exhibits both favorable material properties and excellent biocompatibility. Its unique structure facilitates cell adhesion, spreading, and long-term survival, thereby ensuring good biocompatibility. Furthermore, its intrinsic piezoelectric effect holds the potential to simulate the bioelectrical signals of bone tissue within a mechanical environment in vivo, thereby promoting bone growth and repair. In summary, this scaffold represents a highly promising candidate material for smart bone repair.

TARGETED DELIVERY OF SSRIs VIA NANOPARTICLES FOR SERT MODULATION IN THE GUT EPITHELIUM

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Serotonin (5-HT) is a neurotransmitter that carries messages between nerve cells. Lack of serotonin is associated with depression and other medical conditions. Selective serotonin reuptake inhibitors (SSRIs) are developed to maintain the necessary serotonin level in the body. They block the serotonin transporter (SERT), limit serotonin reuptake and keep serotonin available as chemical messengers between cells. However, SSRIs often cause systemic side effects due to their widespread action. While known for its importance in neurons, SERT is also present in intestinal epithelial cells and has been recognized as a key component of the gut-brain axis. This study explores loading SSRIs onto nanoparticles for targeted delivery to SERT in the gut epithelium, aiming to enhance treatment specificity and efficacy while reducing side effects.

Pharmacokinetic comparisons between an SSRI (citalopram) and its derivative JJC12-13 revealed that JJC12-13 achieved higher concentrations in intestinal and colonic tissues at 1 hour post-gavage, indicating efficient gut absorption and stronger SERT binding. However, citalopram displayed higher brain accumulation over time, reflecting greater central nervous system (CNS) penetration. Despite improved intestinal targeting, JJC12-13 still exhibited systemic distribution, underscoring the need for a localized delivery approach. Mesoporous silica nanoparticles (MSNPs) were then used as gut-targeting carriers for SSRIs, with targeting achieved simply through oral delivery placing them directly in the gut and their limited epithelial permeability keeping them there, while providing 20 percent drug loading and controlled release.

These findings suggest that MSNP-based SSRI delivery could enhance gut-specific SERT modulation while minimizing systemic exposure. Future work will assess the in vivo efficacy, safety, and behavioral outcomes of SSRI-loaded MSNPs to advance a more localized antidepressant therapy.

Construction of self-assembled protein-polymer conjugates for enamel repair

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Key words: Protein-polymer conjugates, Self-assembly, Enamel repair, Remineralization

Abstract: Inspired by nature's sophisticated protein machinery—where self-assembly creates highly ordered nanostructures—researchers design artificial protein-based nanomaterials. Among these, protein-polymer conjugates integrate native protein activity with synthetic polymer versatility. We combined site-specific protein modification with advanced polymer chemistry to develop an innovative self-assembly approach: site-specific *in situ* polymerization-induced self-assembly (SI-PISA). This method enables diverse protein self-assembly systems that preserve biological activity while significantly enhancing pharmaceutical properties, including pharmacokinetics, tumor targeting, and antitumor efficacy. Building on these advances, we expanded its applications. This talk will also briefly introduce our recent work using protein self-assembly as a remineralization template for enamel repair. The resulting material achieves excellent restoration in rat oral cavities by closely matching natural enamel in structure and mechanical properties. Additionally, it exhibits enhanced antibacterial/acid-resistant properties post-remineralization, along with good biocompatibility.

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CARRIER-FREE NANO-ANTICOAGULANT BASED ON A LOW MOLECULAR WEIGHT HEPARIN-LIPID CONJUGATE WITH ALBUMIN-MEDIATED SHUTTLING

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Heparin is a widely used FDA-approved anticoagulant with a market size of approximately 5 trillion KRW. Among various types of heparin, low-molecular-weight heparin (LMWH), derived from unfractionated heparin (UFH), is widely utilized due to its enhanced anticoagulant efficacy, prolonged duration of action, and extended half-life. While the long-term effects of LMWH offer significant benefits for patients undergoing preventive therapy, achieving sustained activity remains a major challenge. In this study, we designed and evaluated a nanoengineered LMWH-octadecylamine conjugate (LMHO) that maintains approximately 97 ± 3% of LMWH activity through site-specific conjugation at the reducing end, ensuring prolonged anticoagulant action. LMHO self-assembles into nanoparticles with an average size of 127.1 ± 0.7 nm in aqueous solution without requiring an additional nanocarrier and binds to serum albumin, facilitating a lipid-based albumin-mediated shuttling effect. This conjugate can circulate in the bloodstream for 4–5 days. We validated the self-assembly capability of LMHO and its interaction with albumin through molecular dynamics (MD) simulations and transmission electron microscopy (TEM) analysis. This innovative carrier-free polysaccharide delivery system, enhanced by nanoengineered albumin-mediated shuttling, presents a promising platform to overcome the limitations of conventional anticoagulant therapies.

Environment responsive nanoplatforms for targeted cancer therapy

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Despite advancements in tumor microenvironment-responsive delivery systems, the range of stimuli for cargo release remains narrow. This study integrates a DNA nanothread-cloaked nanoparticle system and an enzyme-responsive metal chelator-based delivery system to target reactive oxygen species (ROS)-rich and enzyme-overexpressing tumor microenvironments, offering a promising theranostic approach for cancer treatment and imaging. DNA nanothread-cloaked nanoparticles (DBNP) were developed for ROS-rich tumor microenvironments. Using rolling-circle amplification, DNA nanothreads were synthesized and complexed with branched cyclam ligand-modified nanoparticles (BNP), encapsulating the hydrophobic anticancer drug omacetaxine. The ROS within the tumor microenvironment selectively degraded the DNA nanothreads, exposing BNP and allowing for enhanced uptake by ROShigh LNCaP cells, unlike ROSlow fibroblast cells. Molecular imaging confirmed that DBNP exhibited superior distribution to tumor tissues compared to conventional nanoparticles. Ex vivo mass spectrometry showed targeted omacetaxine metabolite accumulation in tumors of DBNP-treated mice, resulting in an 80% reduction in tumor volume upon intravenous administration. An enzyme-responsive metal delivery system (Gd@ErMC) was designed for tumor-specific imaging. Gadolinium (Gd) was loaded into enzyme-responsive macrocyclam (ErMC) conjugated with a PEGylated enzyme-cleavable peptide. This PEGylated shell prevented non-specific accumulation in circulation, enhancing the half-life of the contrast agent. Once at the tumor site, enzyme activity selectively cleaved the PEG shell, releasing Gd and enabling targeted MRI and PET imaging. In vivo imaging of Gd@ErMC in tumor-bearing mice showed extended circulation time, high tumor specificity, and enhanced safety, as confirmed by histological and serological analyses. Together, these findings highlight the potential of combining DNA-masked nanoparticles and enzyme-responsive metal chelators as a dual-functional platform. This platform not only provides ROS-triggered drug release but also facilitates tumor-specific imaging, paving the way for a theranostic approach in MR-guided cancer treatment.

Combinational Prodrug Nanotherapy Validated In a Brain Organoid Model of Alzheimer's Disease

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Drug delivery to central nervous system (CNS) is still challenging in treating neurodegenerative diseases such as Alzheimer's disease (AD). Here, we developed combinatorial prodrug conjugates of galantamine and memantine and incorporated with different neurotranmitter-lipids to formulate lipid nanoparticle (LNP), enhancing CNS delivery and therapeutic efficacy. Two drug molecules were individually linked with enzymatically cleavable ester or amide bonds, by simply reacting with fatty acids consists of different hydrocarbon chains in flow, resulting in two types of single-prodrugs. Alternatively, a dual co-prodrug, covalently linked two drug molecules with two cleavable bonds and hydrocarbon, was newly synthesized by 5-stepwise of flow reaction processes in a high purity and yields. The formulations were systematically evaluated using a brain organoid-based drug screening platform that mimics AD pathology and barriers via endothelial cells and a Transwell system. Subsequently, dual co-prodrug LNP most effectively preserved neuronal integrity and mitigated disease-associated degeneration and AD-related pathological markers, including amyloid-beta and phosphorylated Tau within brain organoids. These findings highlight the potential of dual co-prodrug derived combinational drug delivery systems as a promising CNS therapeutic approach and intervention in neurodegenerative diseases, validated through our integrated human drug screening platform.

Biosketch of Presenter

Prof. Kim is a Changjiang Scholar of HIT-Shenzhen, leading to innovative microfluidics for advanced theranostics from 2025, by shifting from POSTECH in Korea. He obtained Ph.D. in chemistry, post-doctor at materials engineering, and work at national lab and university side for over 30 years in total since 1993. His career on the microfluidic-based continuous-flow synthetic processes covers the manufacturing of API and bespoke drug delivery systems, recently, Al-based autonomous and integrated process of biopharmaceuticals. He has published 350 peer-reviewed papers and 50 patents. He received Academic Excellence Award (2017, Korean Chemical Society), Severo Ochoa Visiting Fellowship (2017, Spain), POSTECHIAN of the Year (2016, POSTECH), The Scientist of the Month (2016, NRF), Yonsan chaired professor(POSTECH,2017), Henry McGee Lecturer (Virginia State Univ, 2021)

In Vivo Macrophage Reprogramming via Biomimetic Membrane Protein Transfer Nanotechnology

ABSTRACT

Cells can expand their functional repertoire by directly acquiring foreign membrane proteins from membrane-based counterparts without genetic alterations. Leveraging by this natural process, we developed a biomimetic technology that uses cell membrane-coated nanoparticles to reprogram cell function through the direct transfer of membrane proteins. Specifically, we found that macrophage membrane-coated nanoparticles, featuring a stiff nanoparticulate core and cholesterol-enriched membranes, effectively transfer membrane proteins *via* membrane fusion. Using this robust technology, we transferred functional membrane proteins *in vivo*, thereby reprogramming macrophages and ameliorating inflammation in a murine colitis model. Extending this approach, we fabricated hybrid membrane-coated nanoparticles derived from macrophages and CHO cells to transfer the zinc transporter 1 (ZnT1) into macrophages, effectively combating secondary infections in septic mice. This work establishes cell membrane-coated nanoparticles as a versatile and mechanistically defined platform for direct membrane protein delivery, bypassing transcriptional and translational processes, and highlights their potential for advancing macrophage-targeted therapies.

Keywords: Membrane protein transfer, membrane fusion, cell membrane-coated nanoparticles, engineered macrophages, sepsis, colitis

Multi-Physical-Field Driven Smart Nanozymes for Precision Medicine Diagnosis and Therapy

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Nanozymes, owing to their high stability, ease of functionalization, and ability to catalyze the generation of reactive oxygen species (ROS), have demonstrated great potential in cancer therapy and antibiotic-resistant bacterial infection control. They can effectively kill tumor cells and bacteria while offering the potential for targeted delivery and integration of multimodal therapies. However, nanozyme therapeutic systems still face multiple challenges in clinical translation, including insufficient targeting, lack of exogenous regulation of catalytic activity, limited real-time tracking with single imaging modalities, and poor stability due to complex platform structures. Notably, there is a lack of a system design that integrates "therapy-monitoring-feedback." To address these challenges, this study designs a photoacoustic-magnetic integrated multifunctional nanozyme platform. By organically integrating magnetic resonance imaging (MRI), photoacoustic imaging, magnetothermal/photothermal/sonodynamic therapy (MHT/PTT/SDT), and nanozyme catalytic functions, the platform achieves deep targeting accumulation, on-demand activated therapy, and multimodal high-resolution imaging. The research results show that the platform significantly enhances local treatment efficacy and imaging accuracy in triple-negative breast cancer, glioma, and MRSA infection models, while improving the survival rate of animal models, demonstrating comprehensive advantages far beyond traditional therapies. In conclusion, the photoacoustic-magnetic integrated nanozyme platform, by integrating multiple therapeutic modes into a single platform, overcomes the limitations of single-treatment approaches and provides a new solution for enhancing diagnostic and therapeutic targeting and controllability. It lays a solid foundation for the construction of next-generation integrated medical diagnosis and therapy systems.

Keywords: Nanozymes; Photoacoustic-Magnetic Response; Cancer; Bacterial Infection; Medical Diagnosis and Therapy

An Orally Administrated Platform for Targeted Therapy of Inflammatory Bowel Disease

Design of an orally administrated platform that can carry drugs targeting the suppression of intestinal inflammation while modulating gut microbiota would be attractive. Here, we have developed an orally administered biomacomolecular complex (cPSM@PNPs) for ulcerative colitis therapy based on food-derived protein nanoparticles encapsulated with anti-inflammatory curcumin (PNPs), with protective effects of core-shell porous starch microparticles (cPSM). The self-assembly of amylose-like polymers created size-controllable shell that resisted the degradation of PNPs in gastric tract, enabling the sustained release of PNPs in the colon. In ulcerative colitis mouse models, orally administered cPSM@PNPs accumulated in the colon and attenuated colonic inflammation by the suppression of TLRs signaling. The fermentation of cPSM in the colon maintained gut microbial homeostasis and produced short-chain fatty acids that regulated epithelial signaling and luminal nitrate availability via peroxisome proliferator–activated receptor–γ. Collectively, this work suggests a promising strategy for the management of intestinal diseases.

Precision Regulation of Nanozyme Activity: From Structural Design to Therapeutic Translation

Nanozymes hold great promise for redox-related biomedical applications, yet their efficacy is limited by intrinsic multi-enzyme activities, competing reaction pathways, and poor controllability in complex physiological environments. To address these challenges, we established a systematic strategy for precision modulation of nanozyme catalytic activity, integrating active-site engineering, microenvironment-responsive activation, and cascade catalytic design. We first developed an active-site engineering strategy to achieve single-pathway catalytic selectivity. By modulating the coordination environment of heme-like Fe–N4 centers with sulfur donors, we constructed Fe–N4S nanozymes exhibiting exclusive peroxidase-like (POD) activity while suppressing catalase-like (CAT) activity. Electronic structure analyses revealed that sulfur coordination elevates the HOMO level and lowers the reduction barrier, enabling the selective conversion of H2O2 to •OH rather than O2, thereby enhancing ROS-mediated tumor sensitization. In parallel, we established a microenvironment-responsive strategy to regulate catalytic pathways using delivery-mediated pH activation. PVP@Pt nanozymes exhibit CAT activity at neutral pH but switch to POD activity in acidic compartments. Utilizing this property, we designed a proton-driven deformable nanozyme that expands and exposes catalytic sites under acidic conditions, enhancing dendritic cell uptake and enabling ROS-triggered immune activation within lysosomes. This demonstrates that delivery-pathway engineering can achieve conditional catalytic selectivity in vivo. Beyond single-enzyme regulation, we constructed multi-enzyme cascade systems to overcome the limitations of isolated catalytic steps under pathological conditions. These include: (i) a CAT–NOS dual cascade that simultaneously generates O2 and NO to remodel hypoxic tumor microenvironments and sensitize radiotherapy; and (ii) a thermally-gated GOx–POD–CAT cascade that couples metabolic disruption with ROS amplification under mild photothermal conditions. These cascades enable spatiotemporally coupled redox reactions and sustained catalytic outputs. Overall, this work establishes a framework for precision tuning of nanozyme catalytic activity across molecular, environmental, and systemic levels, providing a foundation for advancing nanozyme-based catalytic medicine toward controllable activation and disease-specific therapeutic responses.

A Completely Degradable Polydiacetylene Prodrug Enables Months-Long Combination Therapy for Osteoarthritis

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The long-term management of chronic inflammatory diseases like osteoarthritis is hampered by the short half-life of conventional drugs and their inability to specifically target the pathological joint microenvironment. Here, we report a biodegradable polydiacetylene-based prodrug that enables ultra-long-term, on-demand drug release and synergistic microenvironment modulation for over four months from a single intra-articular injection. This prodrug design leverages the reactive-oxygen-species (ROS)-triggered complete cleavage of the polydiacetylene backbone to release the active non-steroidal anti-inflammatory drug while generating benign small-molecule byproducts. The system avoids initial burst release and provides sustained, ROS-responsive drug liberation for more than a month in vitro. In rodent and rabbit models of osteoarthritis, a single injection of the prodrug provided prolonged analgesia, halted cartilage degeneration, and restored joint function. The therapeutic efficacy stems from a synchronized dual mechanism: the scavenging of ROS and the concurrent release of the anti-inflammatory drug, which synergistically reprograms pro-inflammatory macrophages to a reparative state and reshapes the inflammatory microenvironment. This work establishes a paradigm of using completely degradable, conjugated polymer prodrugs to achieve durable, stimuli-responsive combination therapy for chronic diseases.

High-throughput design of Hemoperfusion Platform for Selective Capture of Neutrophil Extracellular Traps in Severe Sepsis

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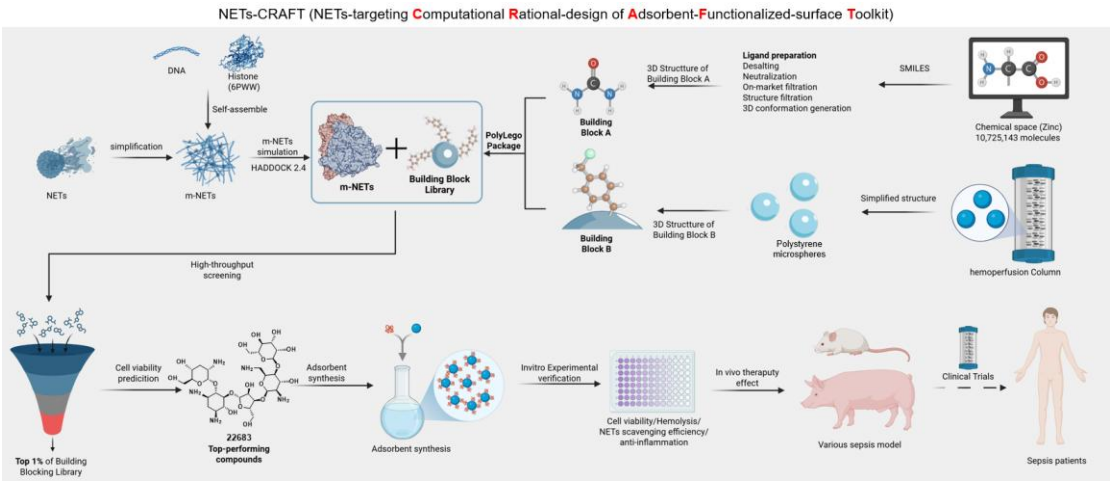
Abstract

Neutrophil extracellular traps (NETs) are emerging as key drivers of sepsis progression, yet their heterogeneous DNA-protein composition obscures how specific NETs features relate to disease severity and limits current high-throughput modeling. Here, we integrate a multi-omics analysis with in vivo validation to link NETs burden and NETs-derived molecular scores to sepsis severity. Guided by these insights, we developed CRAFT, an end-to-end framework for one-stop virtual high-throughput screening and rational design of NETs-targeting hemoperfusion materials. Using CRAFT pipeline, we one-stop engineered PS-Netil, a selective, biocompatible adsorbent that efficiently captures NETs in vitro and in vivo. PS-Netil markedly attenuated NETs-driven inflammation, mitigated cytokine storm, and reduced multi-organ injury, yielding 100% 7-day survival in septic mice and 30-day survival in pigs. Together, our work establishes selective whole-blood hemoperfusion with PS-Netil as a promising therapy for severe sepsis and introduces a one-stop virtual high-throughput screening computational pipeline for designing next-generation biomaterials to address complex molecular targets in sepsis and other systemic inflammatory diseases.



uPAR-Targeted Nanoparticles Delivering Senolytic Drugs (D&Q) Attenuate Vascular Calcification through Selective Clearance of Senescent Cells

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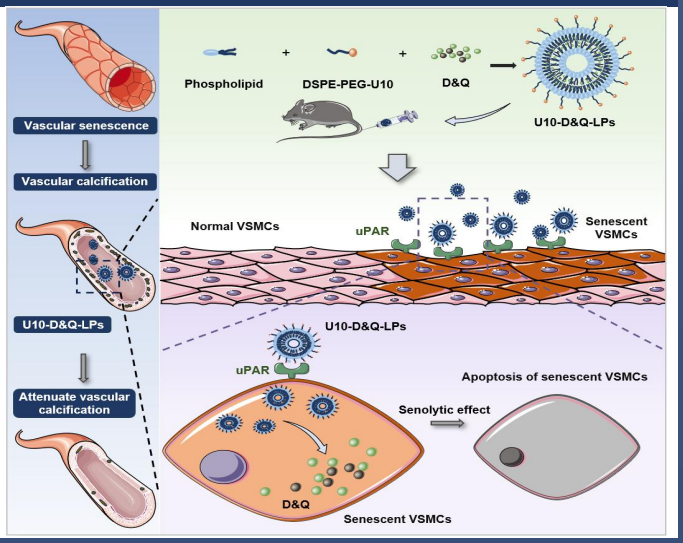
Introduction and Innovation

- Vascular calcification (VC), characterized by pathological mineralization in blood vessel walls, is commonly associated with aging-related diseases including chronic kidney disease (CKD) and hypertension. Currently, **no clinical therapies are available to effectively prevent, delay, or reverse VC progression**. A key mechanism underlying VC is the osteogenic trans-differentiation of vascular smooth muscle cells (VSMCs), **a process accelerated by aging.**

➢ This study **innovatively investigates VC from an aging perspective**. We employed nanoparticle-based targeting of the senescence marker uPAR to deliver Senolytics, specifically clearing senescent VSMCs, thereby suppressing VC development.

➢ Furthermore, we identified **a targeting peptide capable of specifically binding murine uPAR**, overcoming interspecies barriers and offering a valuable tool for translational research.

Abstract Figure



Results

Fig 1 Vessel senescence promotes the onset and progression of VC

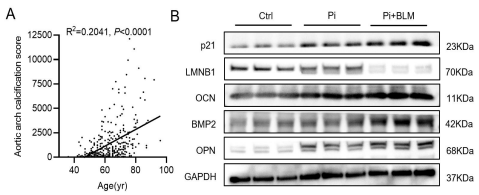


Fig 2 D&Q is the most effective Senolytic drug for eliminating senescent vascular smooth muscle cells and inhibiting VC

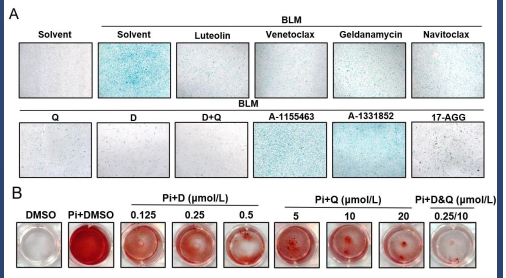


Fig 3 uPAR is highly expressed on the surface of senescent VSMCs

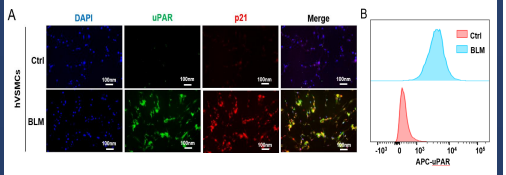


Fig 4 U10 is the targeted peptide we screened that has binding affinity with mouse uPAR

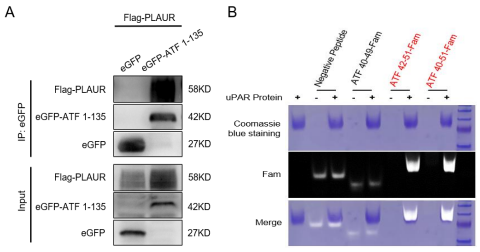


Fig 5 Construction of uPAR-Targeting Nanoparticles U10-D&Q-LPs

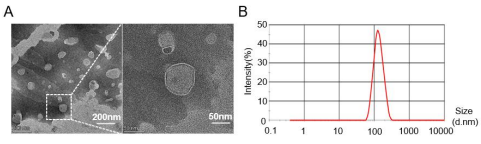
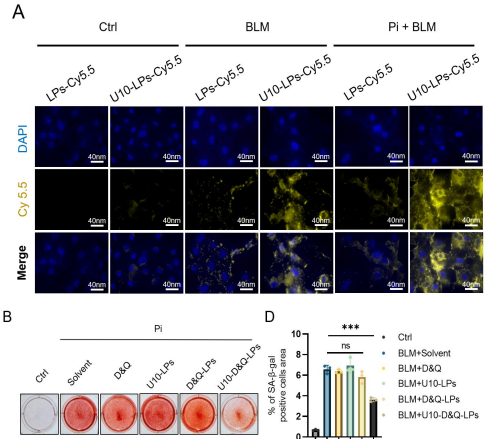


Fig 6 U10-D&Q-LPs can targetedly eliminate senescent VSMCs and inhibit VC



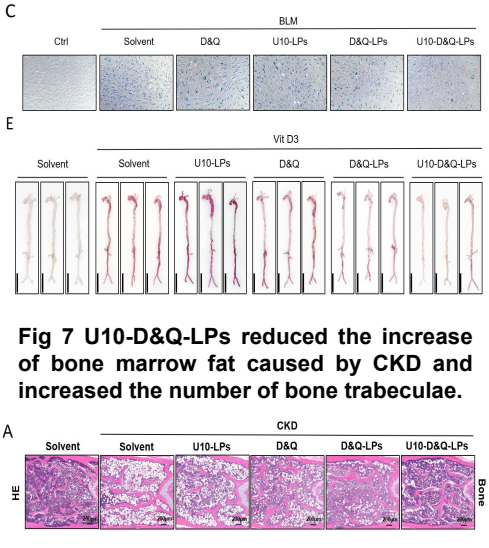


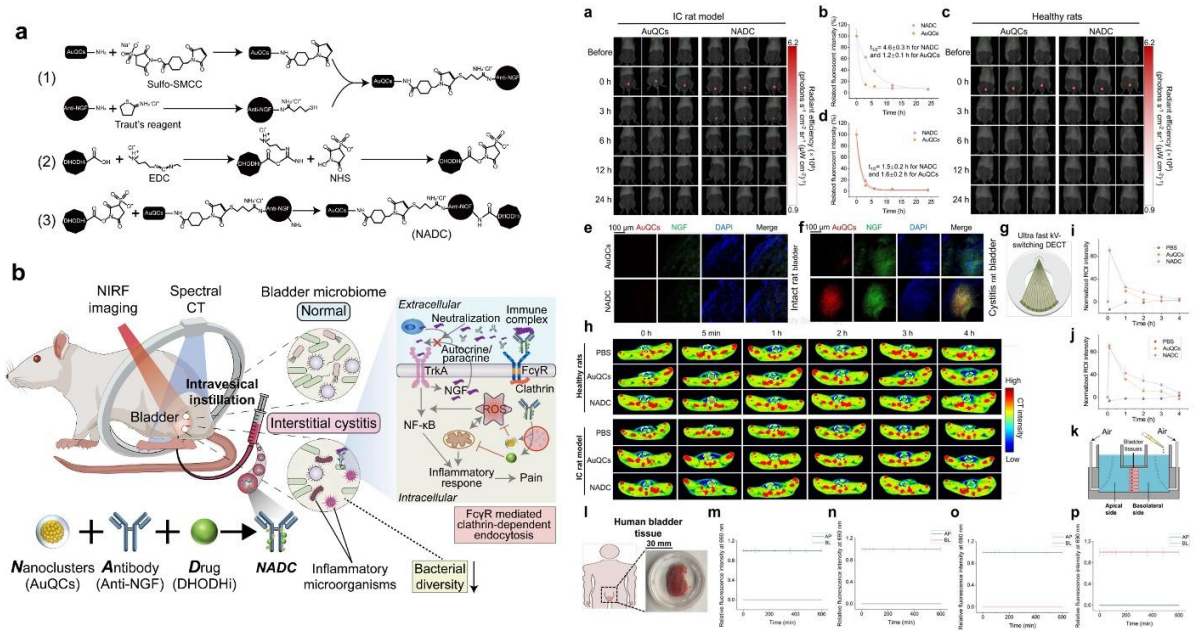
Fig 7 U10-D&Q-LPs reduced the increase of bone marrow fat caused by CKD and increased the number of bone trabeculae.

Conclusion

- uPAR, as a highly expressed marker on the surface of senescent vascular smooth muscle cells, serves as **a new target** for improving aging-related diseases such as vascular calcification.
- By using a nano-drug delivery system to target uPAR and deliver Senolytics drugs D&Q to eliminate senescent VSMCs, It can effectively **reduce the off-target effects of drugs**, alleviate side effects, and **enhance the therapeutic effect.**
- This research provides a safe and effective new strategy for the prevention and treatment of vascular calcification and other aging-related diseases.

Nerve growth factor-targeting nanocluster-antibody-drug conjugates for intravesical precision theranostics of interstitial cystitis

Interstitial cystitis (IC) is a chronic inflammatory bladder disorder lacking timely diagnostic and therapeutic options. Here, we propose a unitary theranostic nanocluster-antibody-drug conjugate (NADC) by covalently attaching dihydroorotate dehydrogenase inhibitors (DHODHi) and ultrasmall gold quantum clusters (AuQCs) to a nerve growth factor (NGF) antagonistic antibody, with multimodality imaging contrasts. Combining anti-inflammatory effects from all individual components, intravesical NADC specifically homed to mucosal lesions with tissue-residing NGF overexpression in the voided bladder, where it neutralized and formed immunocomplexes with secreted NGF to be intracellularly internalized by inflammatory macrophages for payload release through the FcγR-mediated internalization. NADC alleviated inflammation in chronic, acute, and prophylactic IC models of rats, as revealed by behavioral and pathological evaluations. Transcriptomics unveiled cytokine modulation and concomitant inhibition of perturbed IL-17, NF-κB, TNF, and JAK-STAT signaling pathways. Notably, NADC indirectly remodeled the host bladder microbiota by differentially varying anti-inflammatory and pro-inflammatory bacterial diversities. Distinct from conventional nanoparticles conjugated with antibodies and drugs, NADC relies on the antibody framework, outperforms clinical standard-of-care agents, and represents an emerging category of precision theranostic agents with translational potential for IC theranostics in clinical practice.



Title: Engineered Design of Aluminum Salt-Based Nanoadjuvants and Mechanistic Understanding of Their Immunological Potentials

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Abstract:

Aluminum-based adjuvants remain the most widely used vaccine adjuvants, yet their development is constrained by several fundamental challenges, including the difficulty in precise physicochemical control, poor induction of cell-mediated immunity, and an unclear regulatory mechanism for formulation stability. To address these critical issues, our research is dedicated to the engineering design of aluminum adjuvants and the investigation of their immunomodulatory mechanisms, with the goal of advancing the design, development, and application of nano-aluminum adjuvants. We have conducted systematic studies focusing on three primary aspects. Firstly, we designed and developed a library of alum-based nano-adjuvants with well-controlled surface properties and combination adjuvants based on surface modification, elucidating the underlying formation mechanisms for their precise physicochemical control. Secondly, we deciphered the immunostimulatory mechanisms governed by the key physicochemical properties of alum-based adjuvants. Through the innovative design of composite adjuvant strategies, we successfully achieved a potent synergistic activation of both humoral and cellular immune responses. Thirdly, to tackle the challenge of vaccine stability, we established a comprehensive research framework focused on the physicochemical properties that govern the stability of adjuvant-antigen complexes. Our work demonstrates significant progress in the precise design of materials, in-depth mechanistic analysis, and breakthrough composite adjuvant technologies, thereby providing a solid theoretical and translational foundation for the mechanistic study and optimized design of next-generation aluminum adjuvants for vaccines.

Key Words: Aluminum-Based Adjuvant; Nano-Bio Interaction; Immune Response; Structure-Activity Relationship (SAR); Combination Adjuvant; Formulation stability

Local inhibition of NLRP3 in testicular macrophages rejuvenates male reproductive and physical function in aging mice and cynomolgusmacaques

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Age-associated testicular degeneration impairs fertility, disrupts endocrine homeostasis, and contributes to systemic metabolic dysfunction. Despite its clinical impact, effective targeted interventions for testicular aging remain elusive. Immunosenescence has emerged as a key contributor to tissue aging, yet the immunological mechanisms driving testicular decline are poorly understood. Here, we integrated highly multiplexed imaging mass cytometry (IMC) and single-cell RNA sequencing (scRNA-seq) to generate a spatially resolved single-cell atlas of the aging human testis. We identified a proinflammatory axis driven by the cytokine TWEAK, which is secreted from senescent Leydig cells and promotes overactivation of the NLRP3 inflammasome in macrophages. This interaction leads to chronic inflammation, disruption of the testicular immune microenvironment, and functional deterioration of both the endocrine and spermatogenic compartments. To therapeutically target this pathway, we developed a hyaluronic acid (HA)-based hydrogel enabling localized, sustained delivery of siRNA against Nlrp3 (siNlrp3). In aged mice, siNlrp3 hydrogel treatment led to sustained and long-term ablation of NLRP3, suppressed macrophage-mediated inflammation, enhanced the differentiation of steroidogenic Leydig cells, and restored testosterone production, spermatogenesis, and fertility. Notably, this intervention also mitigated the systemic features of androgen deficiency, including sarcopenia, osteoporosis, and adiposity. Therapeutic efficacy was further validated in aged cynomolgus monkeys, demonstrating translational relevance. Our findings uncover a previously unrecognized immune circuit involving NLRP3+ macrophage as a driver of testicular aging and present a targeted strategy for restoring male reproductive and endocrine decline during aging.

TRANSITION METAL-BASED NANOZYME PLATFORMS FOR ALLEVIATING ATHEROSCLEROSIS VIA OXIDATIVE STRESS MODULATION

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Atherosclerosis is chronic and progressive inflammation and remodeling of the vascular wall, involving various cell types and their interactions, including endothelial cells (ECs), immune cells (e.g., macrophages) and vascular smooth muscle cells (VSMCs). Excessive reactive oxygen species (ROS) disrupt redox homeostasis, contributing to the pathogenesis of atherosclerosis. Nanozyme has emerged as a prospective platform for inflammatory diseases management by their intrinsic ROS-scavenging ability and immunomodulatory properties. Yet, providing nanomedicine with demand for targeted delivery and intrinsic antioxidative properties for alleviating atherosclerosis remains challenging.

Noble metal-deposited Nb_2C nanozymes have showed enhanced capability of eliminating broad-spectrum ROS and resolving inflammation in ECs and macrophages via sonocatalytic therapy. One-pot synthesized Fe_3O_4 nanozymes doped with various trace transition metals (e.g., Ce, Mn, Zn and Se) exhibit significantly improved enzymatic-mimicking activity, excellent stability in aqueous solutions, and enhanced biocompatibility. These transition metal-based nanozymes not only modulate VSMCs migration and proliferation but also show a favorable shift from synthetic phenotype toward contractile phenotype.

HF-free etching significantly improves the biocompatibility of transition metal-based nanozymes. Long-term biosafety studies show that noble metal-deposited MXene nanozymes are efficiently cleared from major organs without inducing hepatic or renal dysfunction. Consequently, fluoride-free MXene-based sonocatalytic therapy effectively mitigates advanced atherosclerosis with minimal cytotoxicity. Fluoride-free synthesis eliminates fluoride toxicity, overcoming a major biosafety limitation and expanding the clinical potential of MXene-based nanomedicine for cardiovascular and wound-healing applications. These findings demonstrate the potential of co-functionalized nanozymes as a multifunctional therapeutic platform for mitigating oxidative stress and inflammatory signaling in atherosclerosis. By promoting a contractile VSMC phenotype and inhibiting pathological remodeling, nanozyme-based strategies may offer a promising avenue for targeted intervention and plaque stabilization in cardiovascular disease.

PHOTOTHERMALLY ENHANCING CANCER RADIO-IMMUNOTHERAPY VIA IMPAIRING INTRACELLULAR LACTATE AND DNA DAMAGE REPAIR

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Although radiotherapy (RT) is recognized as a crucial strategy for cancer therapy, it often exhibits suboptimal clinical sensitivity due to the disordered metabolism, activated DNA damage repair (DDR) and low anti-tumor immune response. Photothermal stimulation has been reported to effectively compensate for the treatment of RT-insensitive cells through ameliorating intratumorally blood flow, improving tumor oxygenation status, and thus enhancing radiosensitivity. In this study, multiomics database analysis revealed a significant association between glycolysis and DDR, contributing to RT resistance and poor overall survival outcomes. Hence, a versatile RT sensitizer (GPA) accompanied by photothermal responsiveness is innovatively developed; it not only achieves significant RT sensitization via amplified photoelectric effects, but also impairs tumor lactate metabolism, thus inhibiting NBS1 lactylation under photothermal stimulation, and eventually impedes RT-induced DDR. Moreover, the synergistic effects of photothermal stimulation and RT elicit significant anti-tumor immunity through promoting immunogenic cell death (ICD) and activating the cGAS-STING pathway. The efficient therapeutic effects on both primary and distant tumors indicate that GPA is a potential therapeutic radiation sensitizer, and simultaneously offers a promising option for tumor radio-immunotherapy.

APPLICATIONS OF ZEIN-BASED NANOMATERIALS IN BIOMEDICAL AND FOOD FIELDS

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Here we report the applications of zein-based nanomaterials in the fields of biomedical and food, including tissue engineering, drug delivery, and nutrient encapsulation. In tissue engineering and wound healing, we developed a multifunctional nano-system based on bismuth oxyiodide ($BiO_{1-x}I$) nanoparticles with oxygen vacancies and modified them with polydopamine and ethylene glycol chitosan. This system exhibited pH responsiveness and photothermal/photocatalytic properties, allowing for precise targeting of pathogens and significantly enhancing antibacterial activity, thereby accelerating the healing process in a diabetic wound model. We also developed a self-powered skin patch based on the triboelectric nanogenerator (TENG) incorporating MXene. This patch promoted collagen deposition and angiogenesis through near-infrared photothermal effects and real-time electrical stimulation, while also enabling continuous monitoring of physiological signals. In terms of drug delivery, a brain-targeting nanocarriers were developed using zein and peptides derived from the rabies virus glycoprotein, specifically RVG29, which markedly improved drug delivery efficiency to glioblastoma. Additionally, persistent luminescent nanoprobes composed of elements such as zinc, gallium, and chromium were created, facilitating highly sensitive integrated diagnosis and treatment of brain tumors. In food nanotechnology, to overcome the poor solubility and rapid degradation of bioactive compounds like DHA and quercetin, core-shell structured nanoparticles were formed using natural polymers such as zein, shellac, and chitosan. This approach significantly enhanced their stability and intestinal adhesion in the gastrointestinal environment, broadening the application potential of these functional components. Overall, this series of studies not only demonstrated the feasibility of protein nanomaterials in precision medicine and intelligent nutrition delivery but also established a robust scientific foundation for their future development in personalized treatment, wearable sensing, and food functional enhancement, showcasing extensive translational prospects.

BIFUNCTIONAL HYDROGEL MICRONEEDLE PATCH FOR GLUCOSE SENSING AND TRANSDERMAL DRUG DELIVERY WITH POTENTIAL APPLICATIONS FOR DIABETES MANAGEMENT

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Diabetes mellitus affects over 500 million people worldwide and is among the most common chronic metabolic illnesses. Its treatment often requires frequent blood glucose monitoring and multiple daily insulin injections, which can result in discomfort, poor compliance, and infection risk. To address these concerns, transdermal microneedle systems have emerged as a viable option for painless, minimally invasive, and patient-friendly therapy. Here, we present a bifunctional zwitterion hydrogel microneedle platform capable of both glucose sensing and controlled drug delivery for advanced diabetes management.

A 2D array of microneedles was fabricated using two-photon polymerization (2PP) 3D printing. This array was used as a high-precision master featuring needles protruding from the surface. The master was then replicated in polydimethylsiloxane (PDMS) to make concave cavities in a non-stick mold. This mold was further used for casting a hydrogel photoresist composed of zwitterion monomer, acrylamide, gelatin methacryloyl (GelMA), and lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP). The hydrogel photoresist was photo-crosslinked using ultraviolet (UV) light to fabricate a microneedle patch. The resulting conical microneedles are ~ 800 μm tall and have sufficient mechanical strength for skin insertion. In vitro release studies demonstrated that, after an initial burst, the FD4, the model drug incorporated into the hydrogel matrix, was released according to a near-zero order profile ($R^2 \approx 0.99$) with a constant release rate of approximately 0.49 $\mu g \cdot h^{-1}$, indicating sustained drug delivery suitable for maintaining basal levels. Moreover, the hydrogel matrix exhibited glucose-sensing functionality, as confirmed by the electrochemical measurements, with a limit of detection (LOD) of 7.75 mg·dL-1 and a sensitivity of 8.21 mA·mM-1·cm-2. The bifunctional device provides a potential foundation for closed-loop diabetes management by integrating glucose monitoring with drug delivery. The hydrogel microneedle patch marks a key advance toward wearable devices combining biosensing and therapy, improving patient comfort, treatment compliance, and overall quality of life for individuals with diabetes.

Oral silk protein-adjuvanted nanovaccines target intestinal lymph nodes to simultaneously activate systemic and mucosal immunity against colon cancer

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Abstract

Colon cancer (CC) is a prototypical mucosa-associated malignancy. Beyond systemic immunity, robust activation of mucosal immunity is critical for effective CC immunotherapy. Here, we present a novel particulate adjuvant, the silk fibroin/sericin (SF/SS) complex, which is naturally derived, safe, and capable of simultaneously eliciting systemic and mucosal immune responses. When incorporated into dendritic cell (DC)-targeted mulberry lipid nanoparticles that facilitate intestinal lymphatic transport after oral administration, SF/SS exerts immunoregulatory effect by activating innate immunity through heterodimeric TLR1/2 on DCs via the canonical MAPK and NF-κB pathways, as demonstrated by single-cell RNA sequencing. This activation enhances secretory IgA (sIgA) production through both T cell-dependent and T cell-independent mechanisms in murine and porcine models. When co-administered with tumor antigens, the SF/SS complex induces potent antigen-specific cellular and IgA/IgG humoral responses against malignant CC. Moreover, SF/SS-mediated sIgA production modulates the microbiota-metabolism-immune axis, further amplifying systemic anti-tumor immunity. Overall, our findings establish the SF/SS complex as a promising particulate adjuvant for mucosal tumors by activating both systemic and mucosal immunity.

ENGINEERED EXOSOMES DELIVERING miR-218-5p ATTENUATE ENVIRONMENTALLY-INDUCED PULMONARY FIBROSIS PROGRESSION BY TARGETING FERROPTOSIS-DRIVEN EPITHELIAL-MESENCHYMAL TRANSITION

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Abstract

Pulmonary fibrosis, often triggered by environmental pollutants like $PM_{2.5}$, represents a significant clinical challenge with complex pathogenesis. Epithelial-mesenchymal transition (EMT) is a critical driver of fibrosis progression, frequently associated with dysregulated iron metabolism and lipid peroxidation. Utilizing ferroptosis-modulated models exposed to $PM_{2.5}$, we demonstrate that ferroptosis directly drives EMT in lung tissue. An in vitro macrophage-epithelial cell co-culture system revealed that exosomes derived from $PM_{2.5}$-exposed macrophages induce ferroptosis and subsequent EMT in epithelial cells. Pharmacological inhibition of the key ferroptosis regulator HO-1 reversed EMT alterations. Critically, we identified miR-218-5p as a macrophage-derived exosomal miRNA targeting HO-1 that mediates this ferroptosis-driven EMT. To leverage this finding therapeutically, we constructed engineered exosomes specifically encapsulating miR-218-5p. Systemic administration of these engineered exosomes via nebulization effectively alleviated $PM_{2.5}$-induced pulmonary fibrosis progression in a relevant mouse model. This study provides experimental evidence supporting engineered exosomes delivering miR-218-5p as a novel targeted therapeutic strategy against pulmonary fibrosis driven by ferroptosis and EMT, particularly in environmentally relevant contexts.

Development of a nano-targeting chimera for the degradation of membrane and cytoplasmic proteins

Various targeted protein degradation (TPD) approaches have been developed to overcome the limitations of traditional drug in eliminating pathogenic proteins by exploiting either the proteasomal or lysosomal pathway. However, there is still a lack of design strategies for TPD that utilize two distinct pathways to achieve the degradation of membrane and cytoplasmic proteins. Here, we develop a Nano-Targeting Chimera (Nano-APTAC), which is engineered by covalently attaching the protein-targeting aptamer to graphene oxide (GO) via the amide linkage, to hijack the autophagy-lysosome and ubiquitin-proteasome systems for targeted degradation of membrane and cytoplasmic proteins respectively. In contrast, a mixture of GO and aptamers without covalent interaction has no effect on protein degradation. Furthermore, the in vivo experiments demonstrate the efficacy of Nano-APTACs in depleting targeted proteins and inhibiting tumor growth. The work provides a versatile programmability platform, employing two distinct degradation systems to facilitate personalized design for the degradation of proteins regardless of their localization on the membrane or cytoplasm, and offering potential therapeutic benefits.

DEVELOPMENT OF SMALL PEPTIDES FOR REGULATING NGF SIGNALLING AND BONE REGENERATION

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Abstract

Bone loss is generally the result of trauma and injury, and inadequate bone healing causes functionally debilitating problems for patients, such as a loss of independence and a deterioration in life quality. The nerve growth factor (NGF)/NGF receptor (NGFR) signalling pathway plays an important role in neuronal growth and brain health and has recently been found to be involved in long bone development and health. Human bone marrow mesenchymal stem cells (hBMSC) contribute to the homeostasis of the skeletal system under the regulation of different cytokine profiles, in which NGF was reported to boost BMSC survival and promote BMSC osteogenic differentiation. However, the precise role of NGF/NGFR signalling in bone regeneration remain unclear, because of the lack of appropriate cellular and molecular research tools. Small peptides have attracted increasing attention because of their high specificity, high biological activity, low toxicity, low immunogenicity, and easy metabolism. We previously found that a small NGF-derived peptide (Nsp, the direct binding segment of TrkA), could act as an activator of NGF high affinity receptor, TrkA, and enhanced the calcification of primary human articular chondrocytes (FASEB J 2019, US Patent 11,084,857 B2). Therefore, NGF-derived peptides demonstrate promising potential for modulating NGF signalling pathways and promoting bone regeneration. In this study, leveraging the latest artificial intelligence (AI)-based molecular docking technologies, we designed and screened site mutations of NGF-derived peptide candidates for their binding affinity to NGF receptors. Two peptide candidates were identified and verified with SPR, and the osteogenic enhancing ability of the candidate peptides were then evaluated and confirmed with primary isolated hBMSCs, and with $TrkA^+$ hBMSC cell line (US Prov App 63/621,757)-derived organoids, as well as in a critical size bone defect model in the femoral of adult male rats (n=125). We found stronger calcification and fast bone healing in the peptide treatment groups. This study demonstrated the development of NGF-derived peptides and their therapeutic potential for fast bone regeneration.

pVIII-Engineered Filamentous Phages Trigger High-Avidity Clustering and MSC Mechanotransduction for Stage-Specific Immune Control in Diabetic Peripheral Neuropathy

Non-resolving neuroinflammation is a central driver of diabetic peripheral neuropathy (DPN) and remains refractory to broad anti-inflammatory strategies. Here we introduce an extracellular matrix (ECM)-mimetic, bioinstructive material based on genetically programmable filamentous phages that densely display engineered peptide motifs on the major coat protein pVIII. This design enables high-avidity engagement with mesenchymal stem cells (MSCs), promoting spontaneous assembly into phage–MSC clusters (PMCs) and potent mechanotransduction. PMCs elicit a cytokine-rich, reactive oxygen species-attenuating secretome that constrains inflammation, choreographs a brief innate activation followed by accelerated resolution, and simultaneously promotes angiogenesis. Next-generation transcriptomic profiling revealed mechanotransduction-initiated innate signatures that rapidly transitioned into pro-resolving and regenerative programmes, including axonal extension and amplified neurotrophin signalling. In a diabetic rat model, PMC implantation reduced inflammatory burden and initiated angiogenesis within one week; by four weeks, we observed improved structural and functional nerve repair, enhanced neurovascular regeneration, and mitigation of gastrocnemius atrophy. Collectively, this work advances a genetically programmable, structurally precise ECM-mimetic platform that actively instructs cell behaviours to achieve precision immunomodulation—balancing early innate cues with anti-inflammatory pathways—to restore the neurovascular unit in DPN. The strategy provides a versatile framework for controlling cell fate and immune phase transitions, with translational potential across inflammation-driven degenerative disorders.

Keywords: diabetic peripheral neuropathy, bioinstructive materials, filamentous phages, mesenchymal stem cells, mechanotransduction, precision immunomodulation

A Mitochondria-Specific Nanoparticles for wireless dynamic regulation of Cellular Function in Vivo

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Mitochondria play essential roles in regulating cellular function and fate, making precise modulation of mitochondrial function a promising therapeutic strategy for intractable diseases. Although nanoparticles offer versatile functionalities, such as optical, magnetic and catalytic features, for mitochondrial intervention, their mitochondria-targeting efficacy remains undesirable. Our group develops a new mitochondrial targeting mechanism for the development of mitochondria-specific magnetic nanoparticles. The developed magnetic nanoparticle achieves ultrahigh mitochondrial targeting efficacy (95%) in vitro due to a synergistic Mn^{2+}/TPP dual-targeting mechanism, surpassing conventional mitochondria-targeting nanoparticles, for example TPP-conjugated ceria nanoparticles (~30%), TPP-conjugated PLGA (~50%), etc. Further, the magnetic nanoparticle possesses alternating magnetic field (AMF)-regulated catalase-like activity, enabling real-time precision modulation of mitochondrial function and cellular fate in vivo. Thus, we establish a new platform for remote magnetic regulation of mitochondrial physiology in vivo with broad therapeutic implications.

Translational Research on Functional Nucleic Acid-Based Theranostics

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The pursuit of precision in cancer diagnosis and therapy has driven the development of innovative molecular tools. In this study, we designed a new class of functional nucleic acid (FNA)-based probes integrating diagnostic and therapeutic functions through chemical synthesis and radiometal incorporation. These probes combine the high specificity of nucleic acid aptamers with the physical properties of radionuclides, enabling synergistic tumor targeting and precise energy release at the molecular level. Chemical modifications and structural optimization improved the probes' stability and tumor penetration efficiency.

Mechanistically, the FNA probes operate through a three-step process: (1) Aptamer-mediated targeting of tumor biomarkers; (2) Non-invasive imaging via radionuclide emission for real-time visualization; and (3) Therapeutic irradiation inducing DNA damage and immune modulation. This "recognition–imaging–therapy" strategy establishes a molecular-level balance between diagnostic and therapeutic doses, offering a rational framework for radiopharmaceutical design. The findings define quantitative standards for theranostic dose ratios and elucidate how chemical modifications influence in vivo performance, providing theoretical guidance for future FNA-based drug optimization and expanding their potential in precision oncology and beyond.

A Circuit-Inspired Paradigm for Programming Biological Processes with Modular Nanomaterials

Abstract

The precision of biological systems arises from the ordered sequence of signaling events, much like the function of an electrical circuit is determined by the specific wiring of its components. While this analogy is intuitive, a materials design principle that explicitly engineers functional topology—inspired by the serial and parallel logic of circuits—has been largely unexplored. Here, we introduce such a paradigm. We conceptualize complex biological cascades as circuits composed of discrete functional modules. By constructing nanomaterials where distinct biochemical modules can be physically assembled into prescribed serial or parallel configurations, we demonstrate that the logic of integration is a critical design parameter that dictates biological efficacy.

We validated this principle by reprogramming the antigen-presentation cascade for cancer immunotherapy. A parallel-configured nanomaterial, designed to co-activate antigen processing and immune-stimulatory pathways, profoundly outperformed its serial counterpart, leading to potent tumor regression and antitumor immunity. Crucially, this "circuit-inspired" framework is generalizable. We demonstrate its application beyond oncology by similarly enhancing the precision of intervention in an inflammatory signaling model, achieving superior control over the immune cascade.

This work establishes a modular and programmable materials design strategy that transcends specific biological targets. By prioritizing functional wiring alongside molecular choice, we provide a powerful and extensible platform to engineer smarter therapeutics for a vast spectrum of diseases governed by ordered biological pathways.

MITOCHONDRIAL METABOLISM-REPROGRAMMED NANODRUG ENHANCE TUMOR CUPROPTOSIS

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The active mitochondrial respiration is essential for the tumor therapy, especially for the mitochondrial-depended cuproptosis. Although the hypoxic tumor microenvironment (TME) and Warburg effect severe limit mitochondrial respiration and influence tumor cuproptosis, glucose starvation could act positive roles on activating glucose aerobic respiration. Therefore, reprogramming cells glucose metabolism pathway from glycolysis to mitochondrial oxidative phosphorylation (OxPhos) is essential for improving tumor cuproptosis. Herein, we developed a hybrid tumor cell and plant thylakoid membranes-coated copper-based MOF with conjugation of glucose oxidase (GOx) and lactate dehydrogenase (LDH) inhibitor oxamic acid (TC@OMG). The prepared TC@OMG has good tumor targeting and oxygen production capacities, which is benefit for the mitochondrial respiration. Meanwhile, GOx-induced glucose starvation and oxamic acid-induced LDH inactivation synergetic causing glucose metabolism changing from glycolysis towards mitochondrial OxPhos. Under the special TME with rich of oxygen and less of glucose, the enhanced mitochondrial OxPhos could significantly improve the tumor cells cuproptosis. Specifically, TC@OMG significantly increased basal and maximal respiration and ATP production, while compensatory glycolysis was suppressed and cellular lactate levels was decreased by 82%. It also exhibited 69.67% cells viability inhibition ratio. In vivo study, TC@OMG demonstrated excellent tumor-targeting capability, and upon laser irradiation, it also effectively ameliorated the hypoxic tumor microenvironment (TME) and then amplify cuproptosis. This study provides a novel nanodrug for enhance the mitochondrial-depended cuproptosis and pay a general strategy for other kinds of cancer therapeutics.

POTENT AND SAFE CANCER VACCINE VIA A 'MINIMAL TOXICITY CORE-MAXIMUM STABILITY SHELL' NANOPLATFORM

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Cationic polymers enable efficient mRNA delivery but often cause systemic toxicity at high doses, while lower doses lead to unstable polymer/mRNA complexes. To address this, we designed the "Minimal Toxicity Core–Maximum Stability Shell" nanoplatform. The inner core, composed of biodegradable disulfide-linked reducible polycation (RPC) polymer and mRNA in minimal ratios, minimizes toxicity but is unstable on its own. Encapsulated within a stable, negatively charged CTPCL polymer shell, it forms a core–shell nano-vaccine with excellent in vivo stability and effective endosomal escape. Additionally, avoiding polyethylene glycol (PEG) in the nanoplatform eliminates the risk of PEG-related immunotoxicity. When reduced in the cytosol, the RPC core degrades quickly, releasing the encapsulated mRNA and resulting in high transgene expression. In a B16-OVA melanoma model, this system triggered strong dendritic-cell (DC) activation and antigen-specific T-cell responses without systemic toxicity or anti-PEG antibody production, offering a safe and effective platform for next-generation mRNA vaccines and cancer immunotherapy.

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BIODEGRADABLE ENZYMATIC FUEL CELLS FOR INTESTINAL GLUCOSE SENSING AND CONTROLLED DRUG RELEASE

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Conventional disease diagnostic approaches rely on invasive sampling, both of which are relatively unfavorable and uncomfortable for patients. Ingestible bioelectronic devices hold great promises for real-time health monitoring, disease diagnosis, and personalized medical applications. However, their continuous operation remains constrained by the lack of safe, flexible, and sustainable power sources that can function reliably in biological environments. Biodegradable enzymatic biofuel cells (EBFCs) offer an eco-friendly solution to this challenge by directly converting biochemical energy in the GI tract into electrical energy.

In this study, biodegradable hydrogel is developed as an electrode material for EBFCs, capable of simultaneously achieving self-powered biosensing and controlled drug release. Our strategy employs zwitterionic polymers and multi-walled carbon nanotubes (MWCNTs) to enhance conductivity. Preliminary results demonstrate that the response current increased by approximately 3 times with the presence of glucose substrates. The hydrogel matrix encapsulates both enzymes and drugs within its polymeric network, enabling efficient energy harvesting and sustained drug release while maintaining excellent structural stability and tissue compatibility.

Finally, the hydrogel-based EBFCs will be integrated into a capsule system coupled with a wireless signal transmission module, enabling non-invasive, real-time intestinal glucose sensing and therapy. The system is expected to continuously monitor physiological conditions for up to 12 hours under simulated gastrointestinal conditions. This intelligent hydrogel-based EBFCs provides a sustainable and versatile technological pathway toward next-generation self-powered biomedical devices and integrated therapeutic systems.

Organ targeted cationic lipid nanoparticles engineered through microfluidics for nucleic acid delivery

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Lipid-based nanoparticles have become an essential component in drug delivery systems due to their biocompatibility and applicability. Lipid based carriers are essential for nucleic acid drug delivery, providing protection against degradation and enhancing efficient intracellular transport. It is essential to produce nanoparticles with a uniform structure for safe and effective delivery of drugs and nucleic acids. We used a microfluidic system that can control the size of nanoparticles and minimize batch-to-batch variability. Flow rate and lipid concentration were studied for their effects on the size and polydispersity index (PDI) of nanoparticles. The manufactured nanoparticles were treated with cells to confirm their intracellular uptake, encapsulation efficiency and toxicity evaluation and in vivo biodistribution were analyzed. The optimized flow rate and lipid concentration enabled the formation of monodisperse nanoparticles, which also increased the nucleic acid encapsulation efficiency. In vitro experiments showed that the lipid nanoparticles exhibited high cellular uptake with low toxicity. In vivo analysis further revealed distinct differences in renal clearance between nanoparticles fabricated using the microfluidic method and those produced via the conventional method. Additionally, we sought to develop cationic LNPs with organ-specific targeting capability. To optimize cationic LNP formulations for organ specific delivery, we applied a design of experiments (DoE) approach, utilizing various excipients to optimize formulations. This study suggests the potential of microfluidic lipid nanoparticles as efficient nucleic acid delivery vehicles. Based on this potential, we are engineering lung-targeted cationic LNPs for organ specific delivery.

TITLE: Exploring the Versatile Roles of Inorganic Polyphosphate Materials in Biological Systems

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ABSTRACT: Polyphosphate (polyP), an ancient energy carrier and a compact inorganic polyanionic biopolymer, plays diverse roles in biological systems. Our research has explored its applications in protein phase transitions, microbial metabolism regulation, and nanotechnology, highlighting its potential in bioelectricity generation and nerve cell protection. We first investigated polyP's interaction with positively charged proteins, specifically +36GFP, showing that polyP induces liquid-liquid phase separation (LLPS) and forms protein coacervates through electrostatic interactions. This finding offers new insights into polyP's physiological functions.[1] In nanotechnology, we designed polyphosphate-based nanoparticles (PMNSs) that activated macrophages' innate immune response, suppressing tumor growth. PMNSs induced M1 macrophage polarization, secreting pro-inflammatory cytokines and activating the cGAS-STING pathway. In vivo, PMNSs inhibited tumor growth and activated antitumor responses.[2] Building on this, we synthesized STPE-PMNSs that mimic glutamine synthetase (GS) activity, converting glutamate to glutamine even without ATP. STPE-PMNSs alleviated neurotoxicity in SH-SY5Y cells, providing a new strategy for treating excitotoxic nerve cell damage.[3] In summary, our research highlights polyphosphate's multifaceted roles, from enzyme mimicry and protein phase transitions to microbial metabolism regulation and bioelectricity enhancement. These findings underscore polyP's potential in nanotechnology, protein engineering, and microbial biotechnology, paving the way for innovative applications in science and industry.

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Chiral Neuropeptide Bioprobes-Design and Applications

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Our research focuses on the design and application of chiral neuropeptide bioprobes for cancer diagnosis and treatment. To address critical challenges in precisely identifying pathological lesion boundaries, tracing key functional molecules, and regulating disease progression, we have undertaken interdisciplinary studies encompassing chiral chemical structure design, biological function modulation, and medical applications in lesion boundary detection. First, we discovered that chiral-mutated neuropeptide probes can traverse multiple biological and pathological barriers, enabling precise identification of glioma boundaries. Second, we demonstrated that chiral neuropeptides can modulate the optical and magnetic properties of imaging probes, facilitating the tracing of key functional molecules at tumor boundaries. Third, we established novel methodologies to regulate functional molecular and cellular evolution at tumor lesion boundaries. Currently, our research is expanding to explore the interface between the nervous system and cancer, with a particular focus on how chiral neuropeptides mediate interactions between neurons and gliomas.

Keywords: Chiral neuropeptide, bioprobes, tumor imaging, modulation

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Porosity-Programmed Haversian-like Bone Organoids with Emergent Vascular-Osteogenic Coupling

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Background Large-sized bone organoids are increasingly pursued as physiologically relevant in vitro models for bone development, disease modeling, drug screening, and translational regeneration studies. However, bone development and repair are intrinsically coupled to vascular remodeling, and diffusion-limited transport (~200 μm) makes perfusion-related support essential once constructs reach millimeter scale. In current in vitro systems, endothelial structures often fail to infiltrate early, undergo spatiotemporal rearrangement, and continuously participate in tissue organization. Moreover, many reported "vascularization" approaches either remain small-scale co-cultures or add endothelialized channels at later stages, which is insufficient to recapitulate developmental features where angiogenesis dynamically coordinates osteogenesis. To solve the problem, we developed a structure-driven in vitro platform to engineer large-sized vascularized bone organoids by integrating hierarchical porosity with dynamic channel remodeling.

Methods A biomimetic organic–inorganic bone matrix composed of hyaluronic acid methacrylate (HAMA) and hydroxyapatite (HA) reconstructed the osteogenic microenvironment. A 3D-printed macroscopic framework maintained overall geometry and mechanical stability. Interconnected multilevel channels were generated using gelatin microspheres as sacrificial templates to promote deep cell infiltration and transport.

Results The hierarchical architecture enabled early endothelial invasion beyond the construct periphery and supported progressive reorganization into stable, spatially coupled networks throughout development. Compared with static or single-scale designs, this strategy reduced nutrient gradients, mitigated core necrosis, and synchronized angiogenic and osteogenic programs. The resulting organoids reproduced developmentally relevant features, including "angiogenesis preceding osteogenesis" and coordinated vessel–bone patterning consistent with Haversian-like organization. Functionally, the platform improved in vitro maturation and readouts, enhanced bone-defect repair performance in vivo, and exhibited high sensitivity to vascular-targeting drug perturbations, supporting its utility for mechanistic dissection of angiogenesis–osteogenesis coupling and for translational screening.

Conclusion A 3D-printed, sacrificially templated, magnetically remodelable hierarchical architecture enables developmentally coupled vascular–bone maturation in millimeter-scale bone organoids, supporting mechanistic studies and translational evaluation.

Surface charge of lipid nanoparticles governs stress granule-mediated immune enhancement

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Lipid nanoparticles (LNPs) are the leading delivery platform for nucleic acid vaccines, yet their intrinsic immunomodulatory properties remain poorly understood. Here, we reveal that the surface charge of LNPs is a decisive factor in controlling the magnitude of immune activation through a previously unrecognized mechanism involving stress granule (SG) assembly in dendritic cells (DCs).

We systematically engineered LNPs with tunable surface charges and discovered that cationic LNPs (CALNPs) robustly enhance SG formation by competitively binding to dihydrolipoamide dehydrogenase (Dld), thereby disrupting its interaction with the SG nucleator G3BP1. This charge-driven SG biogenesis promotes DC maturation, enhances antigen presentation via MHC-I, and amplifies $CD8^+$ T cell activation. In tumor-bearing models, ovalbumin mRNA delivered by cationic LNPs induced potent antitumor immunity with the established long-term memory, effectively preventing tumor growth in rechallenge. Notably, CALNPs significantly upregulated DCs populations by over 3-fold compared to neutral or anionic LNPs, and significant enhanced MHC-II expression. Single-cell RNA sequencing confirmed that CALNPs treatment enriched antigen processing and presentation pathways and skewed T cell differentiation toward cytotoxic $CD8^+$ T cells.

Our work establishes a fundamental link between nanocarrier surface charge and immunogenicity, mediated through programmable SG formation. This paradigm shift, from a focus solely on delivery efficiency to harnessing inherent immunostimulatory properties, provides a rational design strategy for next-generation precision nucleic acid vaccines with enhanced immunotherapeutic efficacy against cancers and infectious diseases.

Ultrafast and dilution resistant in-situ gelation hydrogel platform via a molecularly-engineered oxime-crosslinking

The clinical translation of in situ gelling hydrogels for minimally invasive interventional therapies—such as arterial embolization—depends critically on the precise control of gelation kinetics to achieve robust solidification under dynamic physiological conditions. This challenge is particularly pronounced in vascular embolization, where hydrogel formulations must resist substantial dilution and shear stress from blood flow while maintaining excellent biocompatibility for safe intravascular injection. Beyond embolization, these same material properties are crucial for developing effective injectable platforms for drug delivery and regenerative medicine. To address these limitations, we have developed a molecularly engineered protein-based derivative that serves as an intrinsic catalyst, dramatically accelerating a biocompatible crosslinking reaction to form stable hydrogels in situ. This molecular design enables ultrafast, pH-independent, and dilution-resistant oxime ligation gelation even at low polymer concentrations, while endowing the resulting hydrogel with exceptional mechanical stability under physiological shear forces. The resulting robust and biocompatible network is ideally suited to function as a sustained-release depot for therapeutics or a supportive scaffold for tissue engineering. In vitro and in vivo embolization evaluations consistently demonstrate the system's ability to achieve precise and durable vascular occlusion without premature gelation or ectopic embolism, successfully occluding vessels as small as 20 μm. This proof-of-concept in a high-flow environment robustly validates its potential for applications requiring precise spatial control, such as localized drug delivery and minimally invasive tissue repair. With its combination of facile delivery and high biocompatibility, this platform technology offers a transformative solution for a broad spectrum of biomedical applications demanding rapid spatial control.

Biodegradable Piezoelectric Conductive Composite Hydrogel Scaffold: Application in Bone-Cartilage Defect Repair

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ABSTRACT

Objective: Osteochondral injury lacks effective treatments due to the limited self-repair capacity of cartilage. While traditional tissue engineering emphasizes biochemical strategies, it often neglects biomechanical cues. This study develops a biodegradable piezoelectric-conductive hydrogel scaffold that mimics the natural electrophysiological microenvironment to promote osteochondral regeneration.

Methods: This study constructed a bilayer hydrogel scaffold composed of an upper piezoelectric layer based on diphenylalanine-modified dECM (dECM-P) and a lower conductive layer of PEDOT-modified gelatin (Gel-PC). Through gradient freezing, the scaffold forms an interconnected macroporous structure favorable for cell migration. The FF peptide self-assembles into piezoelectric nanostructures, while PEDOT provides conductivity. The scaffold's mechanical and electrical properties were systematically characterized. In vitro studies assessed its promotion of BMSC migration and osteo/chondrogenic differentiation, with mechanisms explored via RNA sequencing. Repair efficacy was further validated in a porcine osteochondral defect model.

Results: Experimental results confirmed the scaffold's efficacy: FF peptide modification boosted the dECM hydrogel's piezoelectric output to approximately 20 mV and 0.8 μA, far exceeding unmodified controls. The bilayer scaffold maintained stable electrical generation over 1000 compression cycles and during in vivo movement. BMSCs migrated effectively on the scaffold, with electrical cues directing them toward chondrogenic differentiation in the piezoelectric upper layer and

osteogenic differentiation in the conductive lower layer. RNA sequencing indicated that this force-electric stimulation acted through Ca^{2+}/PIEZO2-RhoA and TGF-β pathways. In vivo, the D-PC scaffold group achieved superior osteochondral repair at 6 months, showing continuous cartilage and dense subchondral bone in MRI/micro-CT, with histological scores, mechanical properties (nanoindentation), and collagen organization most closely resembling native tissue.

Conclusion: This study successfully developed a biodegradable piezoelectric-conductive bilayer hydrogel scaffold that effectively mimics the natural osteochondral electrophysiological microenvironment. The scaffold promoted directed migration and bidirectional differentiation of BMSCs, demonstrating excellent biocompatibility and significant osteochondral regeneration in large-animal models. This work provides a novel tissue engineering strategy with promising clinical potential for osteochondral defect repair.

KEY WORDS: piezoelectricity, hydrogel scaffold, tissue engineering, osteochondral defect, piezoelectric stimulation

QUANTITATIVE PHASE IMAGING PROMOTING CELL BIOLOGY, BIOMEDICINE, NEW MATERIALS AND BEYOND

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Recent advances in light microscopy have not only fueled the rapid advancement of various research fields in biology, biomedicine, and materials, but also gave rise to several-related industries, thus profoundly improving the life of our human society. Rather than mapping the intensity from absorption, reflection, or fluorescence emission in most of the advanced light microscopy techniques, quantitative phase microscopy (QPM) quantifies the wavefront or phase perturbation from an object over a wide field. Over the last two decades, QPM has been proven to be the next paradigm-shifting imaging method, due to its unmatched advantages, including label-freeness, noninvasiveness, high-precision, high-throughput, and the capability to profile various physical/chemical properties of the specimen in three dimensions (3D). However, its further generalization to many important fields, including cell biological studies, biomedical investigations, and material metrology, is hindered by the system complexity, high unit cost, lack of data interpretation and molecular information, and user-friendly software for targeted specific applications. In recent years, we have tackled the key technical challenges in QPM through a series of innovations, thus enabling QPM's promising potentials in many emerging fields as summarized in the following: (i) break the measurement accuracy limit to sub-angstrom or beyond to measure the hidden electronic-behaviors in atomic structures by developing the Picometer-sensitivity Interferometric QPM (πQPM) and lately the phase amplification microscopy (Φ-Amp); (ii) push the imaging depth limit to millimeter-scale for in vivo imaging of thick tissues by Reflection-mode Optical Diffraction Tomography (rODT) and recently extended to Near-Infrared-II illumination; (iii) beat both imaging and data processing speed limits to realize real-time analysis of large-scale biological cell samples with Express Single-frame Cytometer through Tomographic Phase (xSCYTE) and optical computing; and (iv) establish a comprehensive theoretical framework for precise modeling of phase propagation through strong scatting media. In this talk, we will share our latest technical advances along these directions and their promising applications in atomic manufacturing, brain studies, blood testing, in vitro fertilization, and so on.

FIELD-MODULATED NANOCONFINEMENT STRATEGY FOR CONTROLLED PHASE CRYSTALLIZATION OF GLYCINE TOWARD BIOFUNCTIONAL PIEZOELECTRIC MATERIALS

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Understanding molecular crystallization under nanoscale confinement is essential for tailoring biofunctional piezoelectric materials with defined polymorphism and structural stability. Glycine, the simplest amino acid, crystallizes into three polymorphs (α, β, and γ), with the β-phase exhibiting the highest piezoelectric activity yet remaining metastable under ambient conditions. Conventional nanoconfinement approaches, such as anodic aluminum oxide (AAO) templating, are hindered by discontinuous pore sizes, interfacial perturbations, and difficulties in achieving isolated single-crystal control. Moreover, molecular dynamics simulations capture only short-time behavior, leaving long-term phase evolution unresolved.

To overcome these challenges, we introduce a field-modulated dynamic confinement approach that continuously tunes the nanoscale crystallization environment through spatially controlled field gradients and evaporation dynamics. This method establishes a tunable confinement regime without rigid templates, enabling systematic mapping of β-phase formation across a continuous size spectrum (5-120 nm). Structural and spectroscopic analyses reveal that the interplay between confinement scale, local field intensity, and evaporation kinetics dictates molecular alignment and stabilizes β-glycine formation. A distinct threshold confinement dimension is identified where β-phase nucleation and persistence are maximized.

The obtained β-glycine nanostructures exhibit superior and stable piezoelectric responses with remarkable phase persistence. Their intrinsic electromechanical activity enables efficient conversion of mechanical stimuli into localized electrical signals, providing a foundation for bioelectrical regulation in living systems. This study elucidates the mechanistic principles of amino acid crystallization under dynamic nanoscale confinement and establishes a scalable materials design paradigm for developing sustainable piezoelectric biomaterials with translational potential in implantable and regenerative bioelectronics.

In Vivo Molecular Imaging Based on Intelligent Responsive Magnetic Probes

Guosheng Song, School of Chemistry and Chemical Engineering, Hunan University

Personal Profile：

Guosheng Song, male, is a professor at the School of Chemistry and Chemical Engineering, Hunan University. He received his Ph.D. from Donghua University in 2014 and conducted postdoctoral research at Soochow University and Stanford University School of Medicine from 2014 to 2018. He has served as the corresponding author (including co-corresponding roles) on more than 50 publications, with over 23 of them appearing in high-impact journals such as Nature Materials, Nature Photonics, Nature Biomedical Engineering, Nature Communications, Science Advances , Chem, JACS, and Angewandte Chemie. He serves as an editorial board member for the journals Cell Biomaterials, Chinese Journal of Chemistry, and Med-X. He has been recognized as a Highly Cited Researcher by Clarivate Analytics.

This research systematically addresses the challenges in magnetic in vivo imaging, including insufficient imaging depth, low signal-to-noise ratio, and difficulties in quantitative analysis. By developing superparamagnetic alloy magnetic nanoparticles as imaging probes, the limitation of low magnetization in iron oxide-based particles is overcome, significantly enhancing probe signal intensity. A novel MRI ratiometric imaging method is established to mitigate interference from probe concentration changes on quantitative analysis, providing reliable tools for precise measurement of biomolecules in deeper tissues and for elucidating complex biological effects dependent on biomolecular concentration. These advancements offer powerful tools for early tumor diagnosis, monitoring therapeutic response, and evaluating treatment efficacy.

Representative publications from the past five years are also included：

[1] Zhang X*, Song G* et al. Responsive probes for in vivo magnetic resonance imaging of nitric oxide. Nat. Mater. 2025, 24, 133-142.

[2] Zhang X*, Rao J*, Song G* et al. Magnetic-susceptibility-dependent ratiometric probes for enhancing quantitative MRI. Nat. Biomed. Eng. 2025, 9, 671-685.

Bioelectronic Coupling for Solar-Powered Biosynthesis in E. coli

The fusion of semiconductor materials with non-photosynthetic microbes establishes a functional bioelectronic interface that converts light energy into biologically useful reducing power. However, inefficient charge transfer across the abiotic–biotic junction and the limited coupling of photogenerated electrons with intracellular metabolism hinder performance. Here, we engineer a high-conductivity semiconductor–Escherichia coli interface by uniformly coating cells with densely packed nanoparticles to enable efficient electron tunneling and shuttling. This integrated architecture synchronizes photogenerated charge flow with redox metabolism, resulting in linear increases in intracellular NADH and NADPH levels with rising photon flux. The platform achieves solar-to-hydrogen quantum efficiencies of 13.91 % under full-spectrum and 44.4 % under monochromatic illumination. When combined with engineered metabolic circuits that direct these bioelectronic reducing equivalents into specific pathways, the system enables 11.18-fold higher butanol and 10.88-fold higher lysine production. These findings define a new paradigm of light-driven bioelectronic interfaces that integrate photophysics and microbial metabolism for sustainable solar-to-chemical conversion.

Functional Materials based Platform for Harvesting and Probing Extracellular Vesicle Subpopulation toward Decoding Degenerative Disease

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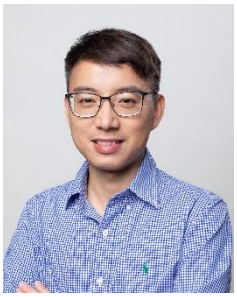
Parkinson's disease (PD) is characterised neuropathologically by α-synuclein aggregation. Currently, there is no blood test that can predict the underlying pathology or offer early diagnosis in the prodromal phase of the disease. We investigated the potential clinical utility of serum neuronally-derived extracellular vesicles (EVs) as biomarkers. Due to the low abundance of neuronal EVs subpopulations and the complexity of the sample matrix, we developed (1) antifouling immunobeads to improve specific EV immunocapture, (2) a multiplexed assay platform to quantify internal cargo proteins in a high-throughput format, (3) digital droplet microfluidic assay to evaluate the EV membrane antigens on single-vesicle level. Such platforms have established a promising PD biomarker based on a-synuclein measurements and offer the potential for the molecular stratification of patients with parkinsonism.

BIOGRAPHY:



Dr Cheng Jiang is an Assistant Professor of BioMedical Engineering at CUHK-Shenzhen. He received his PhD degree in chemistry from the University of New Souths Wales and Postdoc training in Oxford. His research interest is mainly focusing on clinical disease-oriented high/low throughput sensory device-based fundamental and translational study, in which he pioneered to develop and apply antifouling immunobeads to isolate high-purity exosomes from large-scale clinical samples (n>3000) and emphasized the follow-up biomarker discovery-based translational medicine.

He has published > 70 peer-reviewed papers including ***Cell Reports Medicine, JAMA Neurology, Advanced Materials, Advanced Functional Materials, Chemical Reviews, Brain***, etc. He has been also served as guest editor for Photonics, Micromachines, Biosensors and Bioelectronics, and the member of the (Youth) Editorial Board of Extracellular Vesicles and Circulating Nucleic Acids (EVCNA); Brain-X; BME MAT, Nano-Micro Letters, etc.

PYRAMIDAL SUB-NANOMETER OXIDISED NANOPORE: A NEW DEVICE PLATFORM FOR SINGLE NUCLEOTIDE/AMINO ACID SEQUENCING

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Rapid sequencing of DNA and peptides at the single-strand level has been a long-standing challenge. Nanopore techniques, in which sequencing is achieved by monitoring current blockade signals generated as the target chain undergoes translocation across the nanoscale aperture, hold great promise, particularly for long-read sequencing. To date, membrane proteins with the narrowest inner channel of approximately 1 nm remain the sole option for practical nanopore devices. However, biological nanopores are extremely delicate. They have limited chemical resistance and short operational lifetime. Moreover, the k-mer resolution of biological nanopores, which refers to the number of bases each current level may represent, inherently leads to high raw read error rates, thereby difficulty in resolving homopolymers. These shortcomings have significantly impeded their wider adoption beyond research laboratories.

To address the above issues, we have developed a new solid-state device platform featuring a pyramidal sub-nm oxidized nanopore (PSON). PSON is fabricated via batch-mode processing relying solely on wet etching, thus enabling a drastic reduction in manufacturing costs. By utilizing the ultrathin oxide-coated silicon nanopore as an additional electrode, PSON further enables a 3-terminal sensing configuration.

Experimental results demonstrate exceptionally promising performance of our PSON as a single-molecule sequencing platform. The 3-terminal configuration provides a two-fold improvement in signal-to-noise ratio relative to conventional ionic current blockade measurements. Notably, in contrast to biological nanopores, PSON achieves true single-base resolution. Consequently, nanopore sequencing is transformed from indirect inference to direct reading, thereby unlocking the accuracy critical for genetics and epigenetics. Using PSON, we have successfully sequenced ssDNA and peptide samples of various lengths with a raw read accuracy of 95% (i.e., without the aid of neural network models or other algorithms). Leveraging PSON's high chemical resistance, we have achieved real-time monitoring and sequencing of reaction products, specifically, the dissociation of a protein-DNA complex (via *in situ* pH modulation) and the enzymatic digestion of insulin to release its two constituent peptide chains. Furthermore, our PSON prototype exhibits no detectable performance degradation following a cumulative sequencing duration exceeding 150 hours.

AN INNOVATIVE APPROACH FOR SPECIFIC FLUORESCENT LABELING OF NOREPINEPHRINE IN SITU

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Addressed a key scientific challenge in neurotransmitter detection: the three catecholamine neurotransmitters are sequentially biosynthesized *in vivo* and possess highly similar functional groups, which greatly complicates the design of specific molecular probes. To overcome this, they developed an innovative labeling strategy specifically targeting norepinephrine (NE). By capitalizing on the distinctive *β*-hydroxyethylamine motif in NE and employing a tandem cascade reaction with first-generation probes, they achieved breakthrough specificity in NE fluorescence labeling, establishing a new approach for selective NE recognition. Building on this advance, the second-generation probes were engineered to rapidly convert the initial intermolecular recognition event into an intramolecular process, resulting in both enhanced specificity and significantly accelerated reaction kinetics. Notably, the fluorescent products mimic neurotransmitter behavior, allowing dynamic visualization of neurotransmitter release and reuptake processes. Moreover, these probes can cross the blood-brain barrier (BBB), enabling real-time observation of neuromodulatory activity in the living brain. This work provides powerful new tools and valuable insights for NE-related neuroscience research.

Second Near-Infrared (NIR-II) Phosphorescence Imaging

Optical imaging serves as a vital modality in achieving precision medicine, with its progress being fundamentally limited by the challenges in synchronous multidimensional information acquisition and quantitative analysis. Centering on these two key issues, I had proposed the phosphorescent bioimaging in the second near-infrared window (NIR-II, 1000-1700 nm) and developed a multidimensional information coupling and analytical methodology integrating target identification, temporal dynamics, and spatial localization. Some typical achievements had been made as follows. 1) For the first time, I demonstrated the successful red-shifting of phosphorescent emission into the NIR-II biological window (Stokes shift exceeding 400 nm), breaking the fundamental confinement of the energy gap law through molecular engineering. 2) Development of NIR-II phosphorescent imaging technology with ultra-sensitive response ($\Delta pH < 0.4$) to disease-specific targets had been achieved, enabling spatiotemporally resolved mapping of tumor heterogeneity at micrometer-microsecond resolution. 3） The developed methodology had been successfully applied in therapeutic evaluation for patients at Beijing Tiantan Hospital, achieving millimeter-level precision surgery and micrometer-level injury warning. I has published 25 papers as first or corresponding (including co-first/corresponding) author in top journals such as Nat. Biomed. Eng.、Chem. Rev、Chem. Soc. Rev.、Adv. Funct. Mater., supported by National Natural Science Foundation of China and Natural Science Fund for Distinguished Young Scholars of Hubei Province. I had been selected as Hubei Young Top-notch Talent Program. As the third-ranked contributor, I participated in the research program that received the 2024 Hubei Province Natural Science Award Second Class, which recognized groundbreaking advancements in “NIR-II imaging and related biomedical applications”. In future studies of the scientific challenges of precise glioblastoma imaging, I will further boost the application of adaptive-activated NIR-II phosphorescence imaging system, which integrates dual-mode (intensity and lifetime) imaging capabilities to synchronously track critical pathological processes associated with glioblastoma ferroptosis, thereby enabling multiscale correlation of metabolic dysregulation with tumor progression phenotypes.

Telerobotic OCT imaging guided interventions in dynamic luminal organs

Physiological motion within dynamic luminal organs impairs tool-tissue interaction stability during endoluminal imaging and interventions. We present a reconfigurable fulcrum-assisted OCT system for intervention guidance in motile lumens. The fulcrum, constructed from rotationally stacked tubular modules with asymmetric stiffness, achieves nearly tenfold diameter tunability, allowing adaptive anchoring across a range of luminal diameters. In vivo studies in porcine lungs demonstrate that the fulcrum-enabled telerobotic catheter significantly improves OCT imaging stability, achieving motion-free conditions. Moreover, the fulcrum-integrated telerobotic manipulator maintains submillimeter control accuracy in dynamic environments, enabling precise interventions in live porcine models. This robotic fulcrum provides enhanced stabilization without compromising physiological function or safety, ensuring accurate telerobotic imaging and interventions in dynamic luminal settings.

3D Printing of High-Performance Hydrogel Bioelectronic Implants

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Abstract

Hydrogel bioelectronics are emerging as promising candidates for seamlessly bridging biological systems with electronic systems. However, maintaining stable communication between hydrogel devices and biological systems in wet physiological environments remains a critical challenge, largely due to the swelling-induced mechanical degradation of hydrogel encapsulation and electrical failure of conductive networks. To address this, we developed a micellar self-assembly method to fabricate soft, stretchable, and anti-swelling hydrogels as building blocks for implantable hydrogel bioelectronics. Compared with conventional swelling hydrogels and silicones, these anti-swelling hydrogels exhibit significantly reduced foreign body reactions during long-term implantation. By employing a microgel strategy, we engineered the anti-swelling hydrogel into a supporting matrix and a biphasic conductive hydrogel ink, enabling embedded 3D printing of functional hydrogel bioelectronics. Through regulating the monomer diffusion during manufacturing

process, we tailored the conductive phase of the conductive hydrogel, achieving an unprecedented conductivity, reaching up to 4,000 S cm^{-1} and a remarkable strain at electrical failure exceeding 1,300 % when equilibrated in aqueous environment. As demonstrations, we printed different types of hydrogel bioelectronic implants, including brain-computer interfaces, wirelessly powered optoelectronics, and sciatic nerve stimulators. These devices exhibited long-term stability and reliable operation in vivo following implantation in rats. We believe this material system holds enormous promises for advancing next-generation bioelectronics with enhanced biological integration.

Photoresponsive Dyes for Biological Applications

Optical diagnostics and therapeutics based on functional dyes offer advantages such as spatiotemporal controllability, high precision, and minimal invasiveness, yet they face numerous application bottlenecks. Our team has conducted research focusing on photosensitive dyes and optical diagnostics and therapeutics, following a progressive research approach from "intramolecular to intermolecular to in vivo" levels. First, we proposed a design concept for photosensitive dyes based on the regulation of excited-state energy release processes (intramolecular level), revealing the structure-activity relationships and design strategies for dye molecules with highly efficient photoconversion. Thus, we designed and synthesized a series of high-performance dye molecules for optical diagnostics and therapeutics. Second, we established an intermolecular energy transfer enhancement mechanism of "dye-medium-biological target" (intermolecular level), enabling long-lasting labeling or efficient clearance of intracellular targets. This breakthrough overcomes the limitations of traditional photosensitive dyes, which often suffer from poor selectivity. Third, we developed novel technologies for the targeted delivery of dyes in complex biological systems (in vivo level), achieving efficient accumulation and prolonged retention of photosensitive dyes at lesion sites. This advancement overcomes the technical bottleneck of low targeting efficiency in traditional dye delivery systems, enabling breakthroughs in the performance of optical diagnostics and therapeutics for applications such as micro-gland and malignant tumor treatments.

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SIMULTANEOUS PROFILING OF SURFACE PROTEIN AND MIRNA IN SINGLE EXTRACELLULAR VESICLES VIA DNA-WALKER/CRISPR AMPLIFICATION IN DROPLET MICROFLUIDICS

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Early and accurate detection of tumor-derived exosomes remains crucial for precision oncology but is hampered by the inability of conventional bulk assays to capture single-vesicle heterogeneity. Herein, we report a membrane-fusion–mediated, high-throughput digital droplet microfluidic platform capable of dual profiling of surface proteins and intravesicular microRNAs (miRNAs) in single extracellular vesicles (SEVs). Engineered EpCAM-aptamer liposome nanoprobes were designed to selectively fuse with target HER2-positive exosomes, introducing a HER2-responsive DNA walker onto the hybrid membrane and a miRNA-21–activated CRISPR–Cas13a system into the vesicle lumen. Within femtoliter droplet nanoreactors, the DNA walker amplifies surface-binding events into red fluorescence, while CRISPR-Cas13a-mediated trans-cleavage generates green fluorescence corresponding to intravesicular miRNA-21. Digital counting of dual-color droplets enables quantitative single-vesicle analysis with a limit of detection of 10 particles/μL, a sample-to-result time of ~60 min, and throughput exceeding 8×10^3 droplets/s. Applied to plasma samples, the platform achieved an AUC of 1.000, with 100 % sensitivity, 100 % specificity, and 100 % overall accuracy in distinguishing HER2-positive breast cancer patients from healthy donors. This droplet-based SEV fusion and dual-signal detection system provides a versatile and scalable platform for high-throughput, simultaneous analysis of exosome surface proteins and miRNAs for precision cancer diagnosis and point-of-care monitoring.

Peptidyl Liposome for Trigger-Responsive Delivery Vesicle and Smart MRI Contrast

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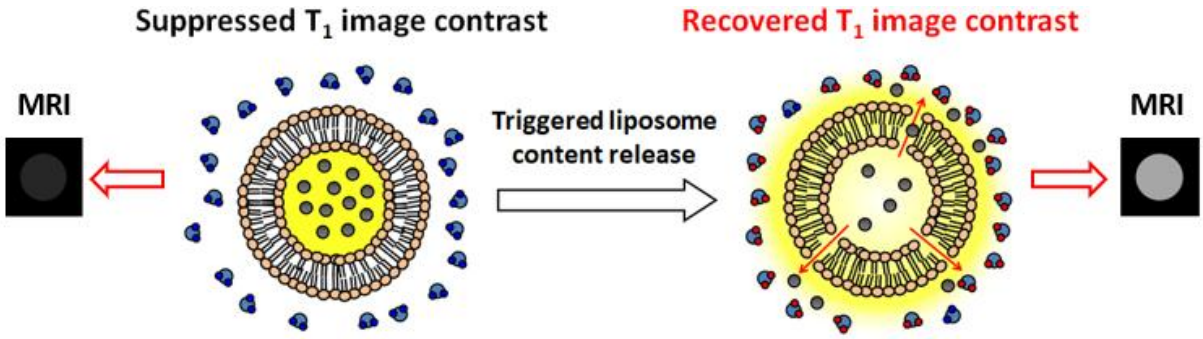
Smart MRI contrast agents that respond to disease-associated biochemical cues offer a powerful alternative to imaging strategies that simply report angiogenic abnormalities. Designing such systems requires liposomal carriers that remain fully silent before activation yet generate a strong contrast upon release. Peptidyl liposomes provide an attractive solution, as membrane-lytic peptides can permeabilize lipid bilayers once their activity is selectively unmasked. However, many peptide-based systems lose effectiveness *in vivo* because activity masking is incomplete or the peptides are activated separately from the liposomes, leading to dilution and weak on-site response. We overcome these limitations by integrating three key elements—peptide activity masking, peptide–liposome conjugation, and release-induced MRI signal amplification—into a single design. The rigid liposomal membrane preserves contrast suppression, while disease-related biochemical cues restore peptide activity, trigger local permeabilization, and activate MRI contrast. This approach enables noninvasive, molecularly specific imaging that moves beyond conventional angiogenesis-dependent contrast mechanisms.

Keywords: liposome, peptide, triggered-release, MRI contrast



NIR-II FLUORESCENCE IMAGING: TARGETING OPTIMIZATION AND BIOMEDICAL APPLICATIONS

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Near-infrared fluorescence imaging in the second biological window (NIR-II, 1000–1700 nm) has emerged as a powerful biomedical imaging modality, offering deep tissue penetration, reduced light scattering, and minimal autofluorescence compared to conventional NIR-I and visible light imaging. This talk presents our recent efforts in optimizing targeting strategies to enhance probe accumulation and specificity-key factors for achieving high-contrast visualization of pathological tissues, particularly in oncology and inflammatory diseases. We discuss the rational design of NIR-II fluorophores, including organic dyes and rare-earth-doped nanoparticles, engineered for improved brightness, stability, and biocompatibility. A central focus is the integration of active and passive targeting approaches, such as nanobody conjugation and surface modification, to promote selective tumor and inflammation site accumulation. We highlight strategies to fine-tune probe biodistribution, circulation half-life, and target-to-background ratios through molecular and nanoscale engineering. Applications in image-guided surgery, real-time monitoring of treatment response, and early disease detection in preclinical models will be demonstrated. By combining advances in materials science, bioengineering, and translational medicine, this work illustrates the potential of optimized NIR-II targeting strategies to advance precision diagnostics and image-guided interventions in modern biomedicine.

MRI-compatible flexible neuroelectronics with bio-adaptive interfaces for brain spatiotemporal analysis at ultra-high magnetic fields

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Abstract

Achieving synchronous neural recording during MRI is essential for high temporal-spatial resolution brain analysis and diagnosis, but conventional devices induce imaging artifacts and radio-frequency heating. Here, we report an MRI-compatible neuroelectronics (MRI-FNe) with bio-adaptive interfaces. Leveraging elastic on-skin and rough implantable recording interfaces, MRI-FNe can adapt to skin and intracranial tissue, forming large-area, stable dry contacts through simple pressure that fills skin texture, while the high surface area of implantable ones enables low-impedance in vivo interfaces—both achieving impedance reductions over tenfold compared to gold films and spin-coated polymer electrodes. Based on these bio-adaptive interfaces, combining proper conductivity and a magnetic susceptibility close to the human body, we achieve artifact-free, safe, and high-fidelity MRI-synchronized neuroelectric signal recording at ultra-high magnetic fields in various scenarios, overcoming the limitations of traditional devices. We demonstrate MRI-FNe for 9.4T implantable and 3T on-skin MRI-synchronized recordings across rodents and humans, enabling spatiotemporal joint analysis of brain function with potential for neuroscience and clinical translation.

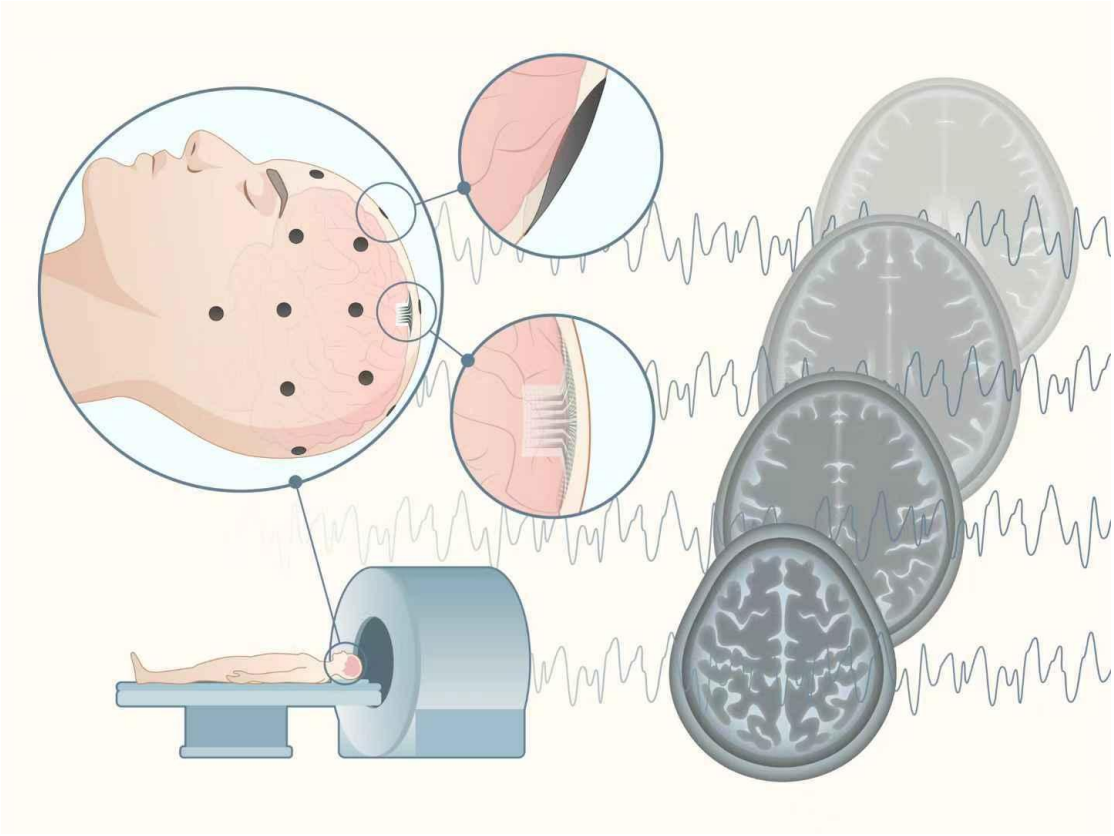

Figure 1. MRI-compatible flexible neuroelectronics with bio-adaptive interfaces.

Schematic illustration of MRI-synchronized neural electrical recording using the MRI-FNe platform. Both on-skin and implantable MRI-FNe enable the synchronous acquisition of neural electrical and fMRI data in regions of interest.

scMIR: A vision–language foundation model for single-cell light microscopy image representation

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Abstract: Quantitative representation of single-cell light microscopy images is essential for advancing cell biology and biomedical research. Most current deep learning approaches are largely task specific for cell representation[1, 2, 3]. Although recent generalist approaches [4, 5, 6] have shown promising results, their vision-only design lacks the complementary biological context required for robust cross-modal understanding, ultimately limiting generalization and interpretability[7, 8, 9]. To overcome these limitations, we introduce scMIR, the first vision–language foundation model for single-cell light microscopy image representation. We curated a large-scale multimodal microscopy dataset encompassing dozens of cell types, hundreds of experimental perturbations, and multiple label-free and fluorescence imaging modalities. Structured textual descriptions were generated for each image to form paired image–text data. scMIR leverages multimodal learning to align visual and textual information, enabling unified representation of diverse microscopy modalities and experimental conditions. Using this dataset, scMIR was evaluated across multiple downstream tasks, achieving up to a 1–15% improvement over existing models in cell-type annotation and demonstrating strong performance in drug perturbation prediction, protein interaction inference. By integrating multimodal learning into single-cell representation, scMIR enables a more biologically interpretable and context-aware representation space, laying the groundwork for holistic cellular understanding and for building virtual cell models capable of emulating cellular behaviors across diverse physiological and perturbation conditions.

Keywords: Light microscopy; Single-cell representation; Vision-language; Foundation model

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Harnessing Toroidal Topology to Regulate Force-Electric Properties and Promote Bone Formation in Biomimetic Nanocomposite Membranes

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Abstract： The rotary plywood structure of natural bone units endows bones with excellent rigidity-toughness synergy, enabling them to avoid fracture through multi-level stress dispersion under impact while providing an ideal mechanical foundation for electrical signal generation. However, existing biomimetic materials struggle to replicate this mechano-electrical coupling mechanism.

This study selected the classical ferroelectric polymer poly(vinylidene fluoride-trifluoroethylene) [P(VDF-TrFE)], known for its solution processability, low cost, and intrinsic flexibility, to fabricate a single-layer face-on lamellar crystal film with a thickness of approximately 100 nm and lateral size of ~20 μm via a dimension-limiting method. In-plane piezoelectric response force microscopy (PFM) characterization revealed a distinct toroidal polar topology within the film. This topological structure not only replicated the mechanical load-bearing behavior of bone but also generated biomimetic electrical signals under external force, achieving for the first time the dynamic coupling of material mechano-electrical properties. Atomic force microscopy (AFM) topography analysis indicated that both the biomimetic membrane and natural bone units exhibit ordered concentric circular structures, forming the basis for mechanical adaptation; PFM responses confirmed their matching circular polarization characteristics, demonstrating a piezoelectric-topological synergistic effect; meanwhile, Kelvin probe force microscopy (KPFM) further revealed that the biomimetic membrane exhibits stable surface potential, uniform negative charge distribution, and close matching with the bone physiological potential, effectively reconstructing the electrical microenvironment of bone defects. Nanoindentation tests showed that the hardness and elastic modulus of the biomimetic membrane were highly similar to those of natural bone tissue, significantly outperforming the control group. Cellular experiments demonstrated that this toroidal polar topology promoted the spreading, cytoskeletal reorganization, focal adhesion maturation, and osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs), while enhancing the clustering of mechanosensing integrin α5. In a rat cranial defect model, this electrical microenvironment significantly accelerated bone repair and integration, with the experimental group forming a dense vascular network by day 7, demonstrating excellent early vascularization capability. This study reveals that implants featuring a toroidal topology can markedly improve osseointegration and angiogenesis, offering a new strategy for optimizing biomimetic electroactive biomaterials in tissue regeneration.

Keywords: P(VDF-TrFE), Toroidal topology , BMSCs, electrical microenvironment, osseointegration and angiogenesis

An Implantable and Degradable Silk Sericin Protein Film Energy Harvester for Next-Generation Cardiovascular Electronic Devices

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Key words: implantable electronical devices, self-power supply, sericin, piezoelectric device, energy-generating

Abstract: Current cardiovascular implantable electronic devices (CIEDs) face a pressing clinical need for the development of battery-free, biodegradable, and biocompatible devices to mitigate the risk of adverse in vivo responses. To address this demand, we propose a natural biomaterial, silk sericin (SS), which exhibits valuable biological activities and contains abundant asymmetric amino acids with adjustable structures, to create an implantable self-powered system based on the piezoelectric principle. The functionalized SS-based piezoelectric film demonstrates a high longitudinal piezoelectric tensor (d_{33}) of 12 pC N^{-1}. An energy-generating device (EG device) utilizing this piezoelectric film can generate electric energy under mechanical force both *in vitro* and *in vivo*. By manually tapping the EG device for a few minutes, the accumulated electricity in a commercial capacitor (1.1 μF) could illuminate LEDs or operate a timer. Furthermore, the instantaneous energy power density (218.5 μW m^{-2}). Furthermore, the instantaneous energy power density achieved by manual pressing the EG device is sufficient to deliver effective pacing to restart a non-beating heart or normalize an atrioventricular block in a preclinical model. Owing to its high biocompatibility and biodegradability in physiological environments, the F-SS-based EG device holds significant promise for the advancement of self-powered power systems for next-generation CIEDs and other implantable and degradable electronic devices.

KIRIGAMI UPCONVERSION PHOTODYNAMIC DRESSING FOR ANTIBIOTIC-FREE CONTROL OF MDR WOUND INFECTIONS

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The global rise of multidrug-resistant (MDR) bacterial infections demands effective non-antibiotic therapies for infected wounds. Here, we introduce a kirigami-engineered, near-infrared (NIR)–activated upconversion photodynamic wound dressing that provides antibiotic-free treatment of MDR infections while simultaneously modulating collagen organization. The dressing is based on a flexible electrospun nanofiber matrix incorporating upconversion nanoparticles (UCNPs) conjugated with photosensitizers. Under NIR irradiation, the UCNPs convert tissue-penetrating NIR into visible light, generating reactive oxygen species (ROS) at the wound surface for localized, on-demand antimicrobial activity without systemic antibiotics.

A key design innovation is the integration of precisely patterned kirigami cuts into the dressing architecture. This structurally engineered layout imparts high stretchability, anisotropic mechanical compliance, and conformal adhesion to irregular or moving skin. As a result, the dressing maintains intimate, stable contact with the wound bed, ensuring uniform photodynamic activation during body motion and improving therapeutic reliability in mechanically dynamic environments.

In vitro, the dressing achieves potent ROS-mediated inactivation of clinically relevant MDR pathogens, including methicillin-resistant Staphylococcus aureus (MRSA) and MDR Pseudomonas aeruginosa. Beyond bacterial killing, the ROS generated within the wound interface induce mild, spatially confined collagen crosslinking, stabilizing extracellular structures and supporting more organized tissue regeneration—thereby enabling a dual antibacterial and matrix-stabilizing function within a single platform.

In infected murine wound models, NIR-activated treatment with the kirigami dressing significantly reduces bacterial burden, accelerates wound closure, enhances granulation tissue formation, and improves collagen deposition, all without systemic antibiotic administration. Collectively, this mechanically adaptive, UCNP-mediated photodynamic system represents a previously unexplored combination of kirigami mechanics and optical nanotechnology for stand-alone management of MDR-infected wounds and highlights a generalizable strategy for architected, light-responsive bioactive dressings.

Frequency-encoded hydrogel robots for multiplexed magnetic control

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Hydrogel-based microrobots show great promise for minimally invasive drug delivery, personalised therapy, and in situ sensing. However, controlling many untethered soft robots inside the body at scale remains a major challenge. Existing magnetic systems typically drive all robots simultaneously and lack simple mechanisms for selective or cooperative control under a single global field.

Here we introduce a frequency-encoded hydrogel robotics platform that embeds addressability directly into the viscoelastic properties of the biomaterial itself **(Figure 1)**. Magnetically responsive hydrogels with dispersed particles are actuated by a programmable Helmholtz coil and exhibit an unexpected multi-peak velocity–frequency response with discrete "active" and "mute" bands. Combined experiments on simplified hydrogel beams, rheology, theory, and finite-element/lattice–Boltzmann fluid–structure simulations reveal the mechanism behind this behavior: frequency-induced stiffening of the hydrogel. As the storage modulus increases with driving frequency, the structural resonance drifts upward and repeatedly re-aligns with the forcing frequency, generating multiple resonant bending peaks and corresponding propulsion maxima.

By tailoring the hydrogel's relaxation spectrum, geometry, and magnetic loading, we design families of hydrogel robots with programmable, non-overlapping or partially overlapping active frequency bands **(Figure 2).** These bands form a frequency-encoding table that supports individual addressing, cooperative actuation, and

reversible magnetic assembly and disassembly of multiple robots—all within a uniform magnetic field. We demonstrate sequential and cooperative cargo transport and modular reconfiguration, showing how frequency-encoded hydrogels could carry different therapeutic payloads, report on local biochemical or mechanical cues, or assemble into temporary scaffolds in response to simple frequency commands.

This materials-based encoding strategy transforms viscoelastic hydrogels from passive carriers into information-rich, actively controllable biomaterials. It provides a scalable route toward multiplexed soft microrobots for targeted drug delivery, combination and personalised therapies, tissue repair, and multiplexed diagnostics and sensing.

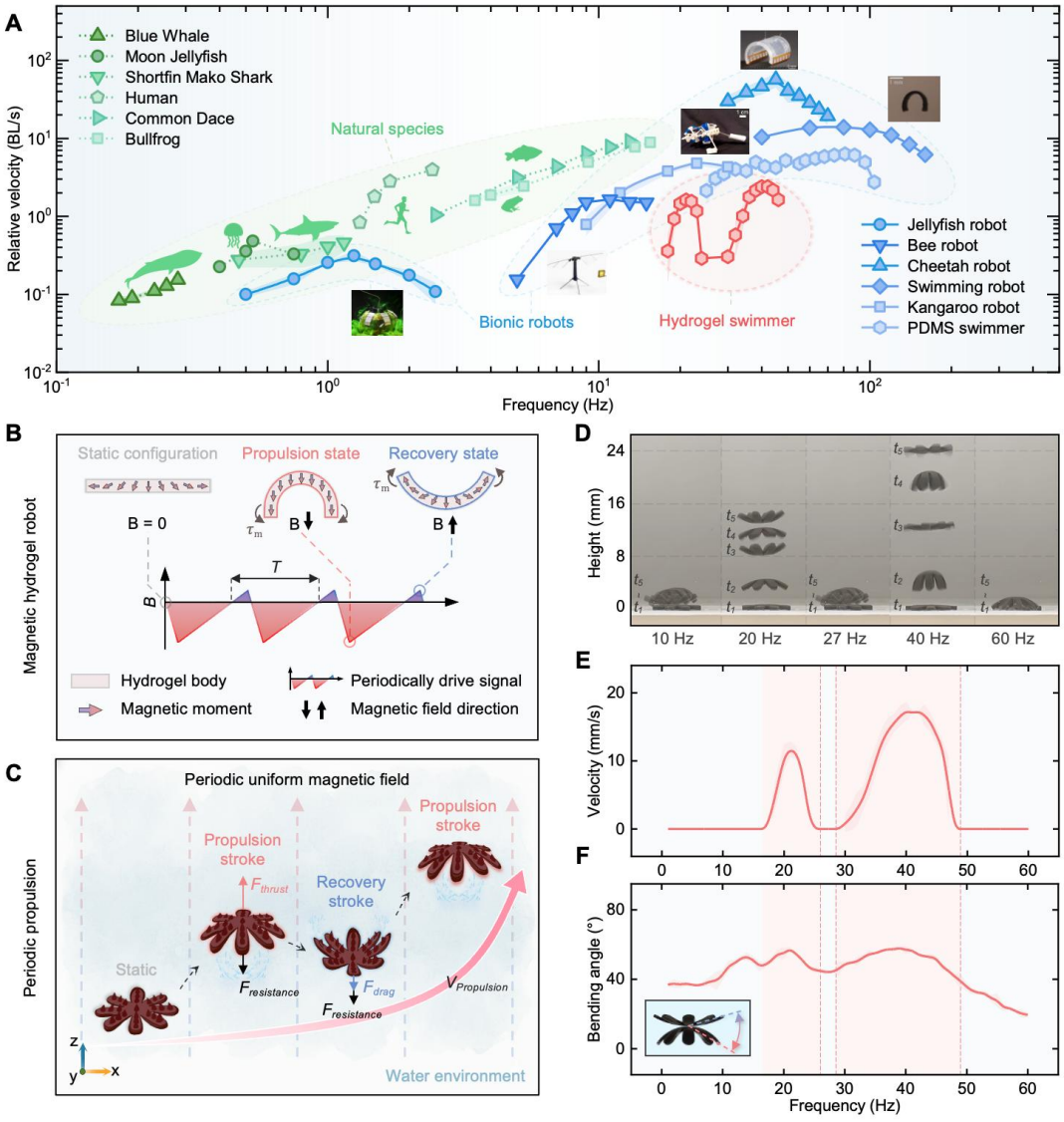

Fig 1. Multi-peak velocity-frequency response in hydrogel robots. (**A**) Comparison

of frequency-dependent relative velocity across natural species (green), bionic robots (blue), and our hydrogel robots (red). Natural species exhibit linear velocity increase limited by muscle contraction. Bionic robots show single-peak responses due to viscoelastic damping. Our hydrogel robots display distinctive dual-peak characteristics with a zero-velocity region between peaks. And PDMS robots with the same shape show single-peak behavior. (**B**) Magnetic actuation mechanism. Periodic uniform magnetic fields drive hydrogel robots with dispersed magnetic particles to bend periodically, cycling through propulsion, transition, and recovery states. (**C**) Propulsion mechanism within a single actuation period. The stronger upward thrust during propulsion exceeds gravity, causing upward displacement, while the weaker backward thrust during recovery results in a smaller downward shift. The net upward displacement per cycle enables continuous swimming velocity. (**D**) Sequential snapshots of propulsion behavior at different frequencies. At 10 Hz, the robot fails to propel due to insufficient thrust. At 20 Hz, it reaches the first velocity peak. At 27 Hz, propulsion ceases as the thrust becomes insufficient. As the frequency rises to 40 Hz, propulsion is reactivated and reaches its maximum velocity. At 60 Hz, the propulsion capability is lost again. (E to F) Dual-peak Propulsion velocity response (**E**) directly correlates with multi-peak bending angle characteristics (**F**). Each velocity peak corresponds to a resonant maximum of bending angle, revealing that the multi-peak Propulsion arises from resonance-driven bending.

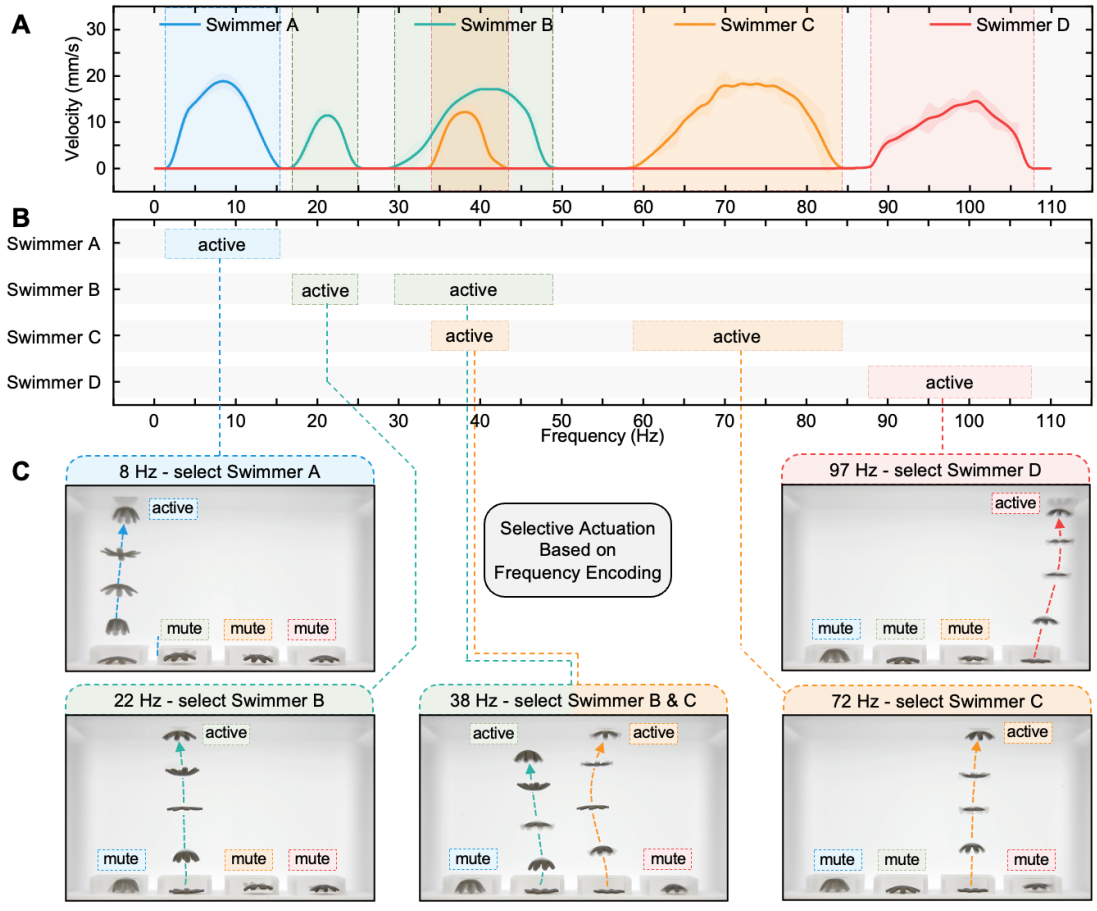

Fig 2. Frequency-encoded selective actuation of multiple robots. (**A**) Propulsion

velocity-frequency responses of four hydrogel robots (A-D). Shaded regions indicate active ranges for propulsion. Robots B and C share an overlapping range near 38 Hz for cooperative actuation. (**B**) Frequency-encoded control table derived from (A), enabling individual or cooperative actuation of multiple robots via frequency switching. (**C**) Demonstration of selective actuation based on frequency-encoded. Robots A, B, C, and D become active individually at frequency ranges of 8, 22, 72, and 97 Hz, respectively; both B and C are cooperatively activated at 38 Hz. Unselected robots remain mute due to insufficient thrust.

Design and implementation of a hyperglycemia-sensing switch for precise glucose regulation

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Abstract

Synthetic gene circuits can be programmed to produce therapeutic proteins in response to the presence of disease biomarkers. Here, we established a hyperglycemia-sensing gene circuit to enhance blood glucose homeostasis in diabetic mouse models. To achieve such a sensing mechanism, we functionally linked the O-GlcNAcylation-mediated nuclear translocation of Yes-associated protein (YAP), a universally existing cellular pathway, to a prokaryotic Tet-Off transcription regulatory system. This linkage involved engineering two chimeric transcription factors that promote high transcriptional activity in response to supraphysiological glucose levels to induce expression of therapeutic proteins from the Tet-inducible promoter. *In vivo* application of the gene circuit enhanced blood glucose homeostasis in diabetic mouse models via coordinating hyperglycemia-triggered insulin or glucagon-like peptide-1 (GLP-1) expression and ameliorated hyperglycemia-induced tissue damage in type 1 and type 2 diabetic mice. Besides its antidiabetic therapeutic potential, the hyperglycemia-sensing gene circuit demonstrates the generalized possibility of repurposing widely-evolved sensors from various organisms for customized therapeutics.

Acknowledgements

This work was supported by the National Key R&D Program of China (Synthetic Biology Research, 2019YFA0904500); the Research Grants Council of Hong Kong (N_CUHK439/24); the Co-funding Mechanism on Joint Laboratories with the Chinese Academy of Sciences (JLFS/M-403/24); and the Innovation and Technology Fund (ITS/020/22MS).

ARCHITECTURE OF SUPRAMOLECULAR PROBES AND THEIR BIOLOGICAL APPLICATIONS

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The tumor microenvironment (TME) is widely acknowledged as a critical factor in cancer progression, profoundly influencing tumor growth, metastasis, and responses to diagnostic and therapeutic approaches. Consequently, strategies aimed at monitoring and intervening within the TME are essential to enhancing diagnostic accuracy and therapeutic efficacy. To achieve adaptive and sensitive monitoring, supramolecular probes have been assembled through non-covalent interactions between primary functional materials and guest molecules, which are expected to facilitate TME monitoring and subsequent intervention. These probes are engineered to respond to unique signals within the TME, such as pH, enzymatic activity, and redox gradients, which are often dysregulated in cancerous tissues. The incorporation of electron-donating or electron-withdrawing functional groups into these supramolecular probes are utilized to participation in redox reactions, which are influenced by the unique oxidative and reductive stresses present within tumors. By tailoring probes to detect redox fluctuations or exploit signaling imbalances in the microenvironment, the selective activation and release of the probes within tumor sites are achieved. The enhanced targeting of the probes improves both sensitivity and specificity, ensuring the precise delivery of their therapeutic or diagnostic payloads, which is crucial for optimal therapeutic outcomes. Owing to their high biocompatibility and responsive adaptability to TME conditions, such supramolecular probes represent excellent materials for the simultaneous monitoring of the TME and targeted therapeutic intervention.

A Closed-Loop Theranostic Probiotic Platform for AI-Powered Home Management of Inflammatory Bowel Disease

Abstract:

Inflammatory bowel disease (IBD) poses a significant healthcare challenge, with current diagnostic methods relying on invasive procedures and specialized equipment that limit accessibility and impose substantial burdens on patients. To address these limitations, we developed an innovative probiotic-based theranostic platform that enables integrated diagnosis and treatment suitable for home use.

Our system features a smart nanocoating that protects probiotics through the gastrointestinal tract and specifically targets inflamed intestinal regions. The coating degrades in response to elevated reactive oxygen species (ROS) levels in IBD microenvironments, releasing fluorescent reporters that are excreted in stool. This process simultaneously mitigates oxidative stress and supports gut microbiota restoration.

A key innovation lies in our AI-enhanced mobile application, which analyzes stool sample images captured by smartphone. Through extensive training on diverse image datasets, our AI model achieves diagnostic sensitivity surpassing conventional clinical methods. This closed-loop platform connects targeted probiotic therapy with AI-powered monitoring, representing a significant advance toward personalized, accessible IBD management.

This study establishes a promising strategy for at-home, patient-centric IBD management by creating a seamless bridge between targeted biological therapy and intelligent monitoring. Furthermore, this closed-loop theranostic approach presents a broadly applicable platform technology that could be adapted for the management of other gastrointestinal disorders.

THE NMD3-PARP1 POSITIVE FEEDBACK LOOP DRIVES THERAPY RESISTANCE IN COLORECTAL CANCER THROUGH ENHANCED DNA DAMAGE REPAIR

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The rapid activation and recruitment of PARP1 is a critical step in DNA damage repair. However, the mechanism by which PARP1 effectively assembles into a functional protein pool at DNA damage sites remains unclear. Here, we demonstrated that the ribosome biogenesis factor NMD3, which is highly expressed in CRC, drives this process by forming a positive feedback loop with PARP1. NMD3 stabilizes PARP1 by competing with the E3 ligase CHFR, whereas PARP1 catalyzes PARylation of NMD3 at the E210 site. This modification is essential for the functional engagement of NMD3 in the DNA damage response and for its role in maintaining PARP1 stability. This feedback loop facilitates the formation of a PARP1 protein pool at damage sites to support efficient DNA repair, thereby reducing cancer cell sensitivity to DNA-damaging chemotherapy. More interestingly, NMD3 binding creates steric hindrance that directly impedes PARP inhibitor binding, mediating resistance to PARP inhibition. Based on this mechanism, we identified a small-molecule inhibitor, Q3, that disrupts NMD3-PARP1 interaction. Q3 effectively dismantles the PARP1 protein pool and removes the steric hindrance towards PARPi, thereby sensitizing tumors to olaparib and standard chemotherapy in vitro and in patient-derived xenograft models. Overall, our study demonstrates a novel mechanism of PARP1 rapid accumulation at DNA damage sites and establishes targeting the NMD3–PARP1 axis as a novel therapeutic strategy to overcome therapy resistance in colorectal cancer.

Keywords: Colorectal cancer; DNA repair; PARP1; Ribosome biogenesis; Synthetic lethality.

Vaccine-Induced CD8+ T Cells Mediate Targeted Immunotherapy of Medial Vascular Calcification

This study establishes a novel immunotherapeutic concept that redirects pre-existing, vaccine-induced memory $CD8^+$ T cells to selectively eliminate vascular smooth muscle cells undergoing osteogenic transformation—the cellular driver of arterial calcification. Traditionally regarded as irreversible and immunologically inert, vascular calcification is here shown to be amenable to immune-based therapeutic intervention. By leveraging the host's own immune memory, this approach enables precise, controllable, and low-cost elimination of pathological cells, providing a practical route to treat chronic vascular disorders. Beyond oncology, this work extends T cell–based immunotherapy to non-malignant diseases, opening new translational opportunities for otherwise untreatable degenerative vascular conditions.

Self-Activating Nanoagents for Precise Antibacterial and Antitumor Therapy

Cancer and bacterial infections currently represent the first and second leading causes of death globally. Conventional therapeutic approaches are often constrained by drug resistance, systemic toxicity, and inadequate targeting precision. There is consequently a pressing need to develop drug-independent treatment strategies. In this context, microenvironment-activating nanoagents offer a promising solution by enabling spatiotemporal control over the "inertia-to-activity" transition of therapeutic agents specifically at the disease site. We have developed two categories of self-activating nanoagents that exploit either the pathological microenvironment of diseased tissues or subcellular compartmental differences. The first category includes a hydrogen sulfide (H_2S)-releasing FeS/Au nanocluster composite nanozyme, which responds to the mildly acidic tumor microenvironment to initiate a Fenton-like reaction, generating reactive oxygen species (ROS) while releasing H_2S as a gassing therapeutic molecule. This dual action synergistically induces ferroptosis and apoptosis in tumor cells. Another gold/iron nanozyme exerts potent antibacterial effects through a glucose-triggered cascade reaction that produces hydroxyl radicals (·OH), with the concomitant release of H_2S promoting infected wound healing. The second category involves a mitochondria- and lysosome-dual-targeting prodrug-like microneedle system. This system capitalizes on the distinct physicochemical properties of these subcellular compartments to achieve site-specific activation of therapeutic agents, leading to enhanced tumor cell eradication. By precisely regulating the transition of nanoagents from an inert state under physiological conditions to a therapeutically active state within pathological niches, this microenvironment-triggered strategy not only minimizes off-target toxicity but also amplifies treatment efficacy through cascaded reactions. These advances underscore the significant potential of nanotechnology in addressing global health challenges posed by cancer and bacterial infections.

Bioengineered Neutrophils for Smart Response in Brain Infection Management

Brain infections, inherently intricate, stand at the intersection of neurology and infectious diseases as an urgent medical challenge. These infections are often coupled with extensive inflammation, rendering the clinical picture even more complicated. Addressing such scenarios necessitate a harmonized approach that not only targets the underlying pathogen but also alleviates the inflammatory sequelae, ensuring comprehensive patient care. However, the treatment of brain infections is fraught with various obstacles. Foremost among these is the blood-brain barrier (BBB). While the BBB serves as both a protector and a gatekeeper of the central nervous system (CNS), its tight junctions and selective permeability unexpectedly hinders the passage of crucial therapeutic agents. This barrier often leaves clinicians struggling to achieve effective drug concentrations within the CNS, thus complicating the management of brain infections.

Recognizing the impediment posed by the BBB, there has been a burgeoning interest in the scientific community to find novel ways to navigate this barrier. A series of drug delivery systems have been developed to enhance BBB penetration, such as peptide and protein vector systems, physical disruption, nanotechnology formulations, and cell-based approaches. For instance, the utilization of peptide and protein vectors has been a topic of keen interest. By linking drugs to these vectors, which can naturally transverse the BBB, therapeutic agents can be delivered into the brain. Beyond biological strategies, there are also physical methods being explored. Techniques such as focused ultrasound have shown promise in temporarily disrupting the BBB, allowing for enhanced drug delivery to the brain. In addition, one of promising avenues has been the application of nanotechnology. Nanoparticles, given their minuscule size, offer the potential to bypass traditional barriers. By modifying the surface of nanocarriers with specific ligands or proteins, researchers can exploit receptor-mediated transport mechanisms to facilitate drug passage through the BBB. Another emerging strategy is the use of cells as delivery vehicles. Notably, neutrophils possess an innate ability to traverse the BBB during infections and inflammation. Leveraging this natural

propensity, scientists are exploring neutrophils-based systems, among other cell carriers, to drive therapeutic agents across the BBB. While each of these techniques offers potential strategies to bypass the challenges posed by the BBB, they come with their own set of complications and limitations, such as immunogenicity, low stability, off-target effects, and complexity of production. Overcoming these will require a combination of innovative research, multi-disciplinary collaboration, and rigorous testing to ensure both effectiveness and safety.

In pursuit of an innovative solution, we exploit the innate ability of neutrophils to act as our "Trojan Horses", developing a sophisticated, dual-responsive delivery system named CellUs (**Figure 1**). This ingenious system utilizes live neutrophils engineered to encapsulate a liposomal formulation containing dexamethasone (DEX), ceftriaxone (CRO), and oxygen-rich perfluorocarbon (Lipo@D/C/P). The use of neutrophils for drug delivery offers numerous benefits, including improved drug stability, targeted delivery, and the potential reduction of systemic side effects. Particularly, neutrophils, endowed with a natural propensity to cross the BBB in the face of infections and inflammation, present a promising vehicle for delivering both antibiotics and anti-inflammatory agents to combat brain infections. Concurrently, liposomal formulations are increasingly popular for their biocompatibility and versatility in encapsulating a diverse array of therapeutic agents, from small-molecule drugs to larger biologics.

In our study, CellUs innovatively encapsulates a distinctive blend of therapeutic agents within the protective domain of neutrophils. This approach ingeniously merges the antimicrobial power of antibiotics with the inflammation-regulating capabilities of anti-inflammatory drugs. Such a combination enables simultaneous treatment of both the infection and its associated inflammatory response. Notably, the inclusion of oxygen supply within this therapeutic strategy plays a pivotal role in enhancing the treatment of brain infections. Adequate oxygenation not only aids brain cells in optimally combatting the infection but also potentially amplifies the efficacy of other therapeutic interventions. For example, the effectiveness of antibiotics and the immune response may be significantly boosted in a well-oxygenated environment. This

comprehensive treatment approach is especially crucial in brain infections, where the restoration of normal function in damaged brain tissue is imperative.

Crucially, as these neutrophils respond to infection and inflammation signals and traverse the BBB, they transport the encapsulated drugs along. Upon reaching the target site, specific triggers, such as inflammatory factors, induce the release of the encapsulated drugs, ensuring their direct delivery to the affected areas within the CNS. The inclusion of perfluorocarbon, an ultrasound-responsive compound, further enhances the precision and control of drug release, enabling the deployment of therapies exactly where and when needed. This dual functionality exemplifies the epitome of precision medicine, where therapeutic delivery is optimized both spatially and temporally.

Through our research, we explore the mechanisms, efficacy, and potential of CellUs, demonstrating its ability to combat *Staphylococcus aureus* (*S. aureus*) infections and associated meningitis in experimental models. Our efforts are directed not just toward facilitating the entry of drugs into the brain but also toward ensuring their targeted and sustained release, thereby optimizing therapeutic efficacy while minimizing side effects. As we unveil our findings, it becomes apparent that CellUs capitalizes on the natural attributes of these immune cells and multidisciplinary collaboration, holding significant promise in revolutionizing the treatment of brain infections and their associated complications.

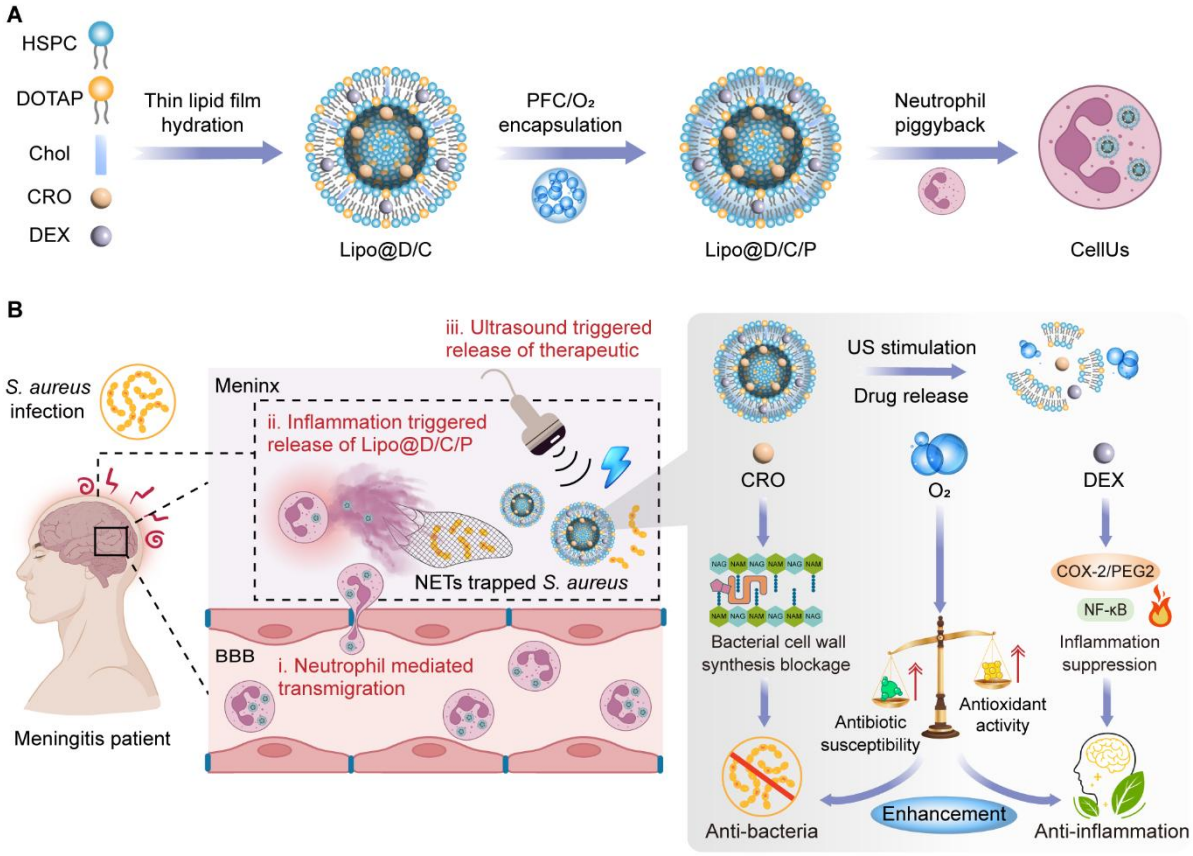

Figure 1. Smart-responsive neutrophils (CellUs) engineered for comprehensive treatment of brain infections. (A) Preparation of CellUs. CellUs is ingeniously constructed by encapsulating a liposomal formulation (Lipo@D/C/P) comprising hydrogenated soybean phosphatidylcholine (HSPC), 1,2-dioleoyl-3-trimethylammoniumpropane (DOTAP), and cholesterol (Chol), antibiotics ceftriaxone (CRO), the steroidal anti-inflammatory drug dexamethasone (DEX), and oxygen-loaded perfluorocarbon (PFC/O_2) within live neutrophils. (B) Treatment of meningitis by CellUs. CellUs inherits the innate chemotactic properties of neutrophils, allowing it to respond to inflammatory factors and migrate across the blood-brain barrier (BBB) to the inflamed meninges. Its selective release mechanism is triggered by inflammation, ensuring efficient and direct delivery of Lipo@D/C/P to the affected sites within the central nervous system (CNS). Crucially, under mild ultrasound stimulation, CellUs can significantly release therapeutics owing to the eruption of perfluorocarbon. This mechanism allows for spatially and temporally controlled release of antibacterial and anti-inflammatory drugs, as well as oxygen effectively, thereby addressing both the severe pathogen infection and associated inflammatory response.

Ultrasound-activated wireless electrical vagus nerve stimulation for treating enteritis

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Abstract: Targeted vagus nerve stimulation provides an opportunity to regulate metabolic homeostasis and suppress inflammation[1-2]. Here, we report wireless, leadless, and battery-free electrical vagus nerve stimulation for the treatment of colitis using an ultrasound-activated piezoelectric fibrous implant. The soft implant presents high mechanical conformability to dynamic motion nerve tissue and can seamlessly wrap around the vagus nerve to convert ultrasound into electrical stimulation, thus eliminating the limitations by battery-powered tethered components and mechanical mismatch at the rigid electrode-soft neural tissue interface. Our results illustrate that ultrasound-activated piezoelectric stimulation precisely modulates the intestinal vagus nerve branch (sacral splanchnic nerve) to active immunoregulation, thereby increasing the resistance of rats to dextran sulfate sodium-induced colitis. This bioelectronic-based remote immunoregulation offers unlimited possibilities for precision medicine.

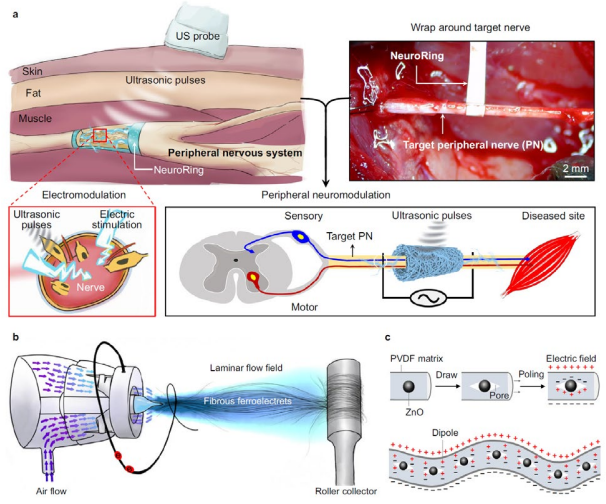

Fig. 1: Concept and material design of ferroelectret-based NeuroRing for peripheral neuromodulation. **a** The NeuroRing wrapped around a peripheral nerve (PN) is an US receiver that can be triggered by US pulses to yield electrical impulses targeting the PNs that regulate various organs and functions. **b** Illustration of the laminar-flow-assisted electrospinning for fabricating ferroelectret fibers. **c** Ferroelectret was a composite consisting of piezoelectric PVDF and ZnO particles with a porous ferroelectret structure. The cavitation effect of the gas stretching force creates voids at the particle-polymer interface. These pores induce electrically polarized domains (dipoles) in a subsequent process called poling. The increased numbers of dipoles improve the output of the electric charges that are formed by US vibrations.

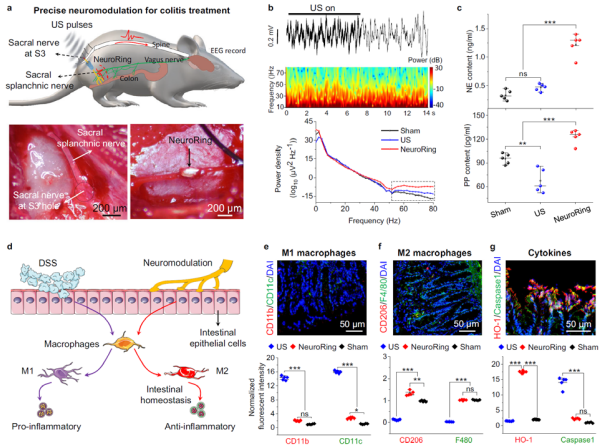

Fig. 2: Sacral splanchnic nerve modulation for colitis treatment. **a** Schematic and microscopic image of the NeuroRing implant that wrapped around the sacral splanchnic nerve. EEG signals were recorded while ultrasound-induced electrical stimulation of the sacral nerves was performed. **b** EEG (top) recorded over parietal cortex and comparison of the power spectrum (middle) and its derived quantified power spectral density (bottom) for sham control, US alone, and NeuroRing showing the significant enhancement in rats treated with ultrasound-induced electrical stimulation. Sham control refers to the sham operation and normal drinking water group. US alone refers to the sham operation and drinking DSS group. Bottom: the black dashed box intuitively reflects the significant enhancement of ultrasound-induced electrical stimulation, especially in the range of 50–80 Hz. **c** Expression levels of NE (sympathetic endocrine hormones) and PP (vagal endocrine hormones) in blood samples. **d** Schematic representation of the protective mechanism of US-triggered NeuroRing in DSS-induced colitis. Neuromodulation alleviates DSS-induced colitis by inhibiting macrophage M1 polarization and promoting M2 polarization. **e** Immunostaining for M1 macrophages represented by CD11b (red) and CD11c (green) of colon tissue. Bottom: the quantification (bottom) of CD11b and CD11c. CD11b. **g** Immunostaining for HO-1 (red) and Caspase1 (green). Bottom: quantification (bottom) of HO-1 and Caspase1.

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THE DEVELOPMENT OF SILICA-BASED DELIVERY RNAI THERAPY FOR PRIMARY HYPEROXALURIA (PH)

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Primary Hyperoxaluria (PH) is a rare autosomal recessive metabolic disorder in which liver produces excessive oxalate. Chronic oxalate overproduction contributes to the development of nephrolithiasis, nephrocalcinosis, and systemic calcium oxalate deposition in severe cases. Current therapies, such as combined liver-kidney transplantation and aggressive hyperhydration, alleviate clinical symptoms but fail to correct the underlying metabolic defect, and many patients still progress to end-stage renal disease (ESRD), highlighting an unmet need for effective therapeutics. To address this, we developed a silica-based nanoparticle (C-dots) delivery system designed to deliver RNA interference (RNAi) targeting *LDHA* highly specific to liver. Lactate dehydrogenase A (LDHA) is a key enzyme in hepatic oxalate synthesis and thus appears as an attractive therapeutic target for PH. C-dots are surface-modified and conjugated with N-acetylgalactosamine (GalNAc) ligands for hepatocyte-specific uptake, and siRNA to downregulate hepatic LDHA expression, thereby reducing oxalate production and mitigating disease progression. The C-dot carrier provides high siRNA payload capacity with hepatocyte-specific uptake and a degradable silica framework that minimizes systemic exposure and immune activation. Our ongoing research has successfully synthesized and functionalized siRNA-GalNAc C-dots and achieved >70% LDHA knockdown in mouse and human hepatocytes with predominant liver biodistribution and minimal off-target accumulation, as confirmed through IVIS imaging and qPCR analysis. Further work will evaluate immune responses, perform in vivo validation in mouse models, and conduct translational assessments to determine therapeutic potential.

Keywords: Primary Hyperoxaluria (PH), RNA interference (RNAi) therapy, siRNA, N-acetylgalactosamine (GalNAc), LDHA, silica-based nanoparticle

Photobiological applications of supramolecular metallophilic interactions

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Supramolecular self-assembled drugs combine the advantages of high reproducibility of small molecule drugs with the passive tumor targeting capabilities of nanomedicines. Our research revealed that metal-carbon bonds can induce an atypical supramolecular force, namely "metallophilic interactions," which promotes the self-assembly of metal complexes into nanodrugs. These nanodrugs can stably exist as nanoparticles in solution, cells, and in vivo in mice, demonstrating the potential for small molecule metal drugs to be directly used as nanomedicines for cancer diagnosis and treatment. This series of studies highlights the important value of metal-carbon bonds in regulating the optical and pharmaceutical properties of metal complexes, as well as the promising applications of metallophilic interactions in photobiology, warranting further exploration.

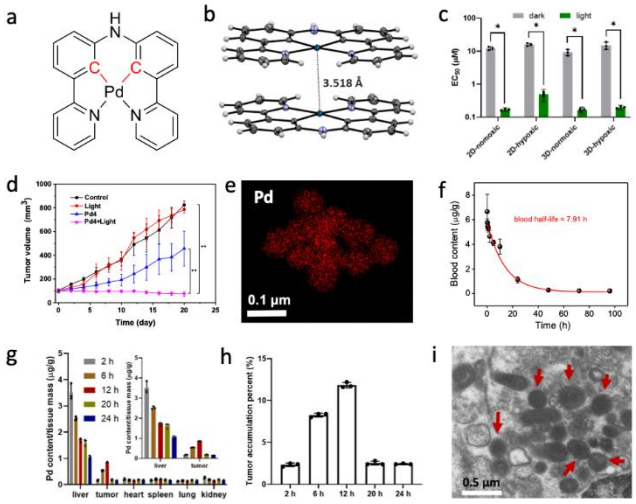

Figure 1. (a) Structure of palladium complex; (b) metallophilic interaction in single crystal state; (c) Comparison of toxicity to cancer cells in different models under photodynamic therapy; (d) Tumor growth inhibition curve in mice; (e) Pd elemental analysis of nanoparticles in blood; (f) Pharmacokinetic curve of palladium complex; (g) Distribution of palladium complex in mouse organs; (h) Enrichment rate of palladium complex in mouse tumors; (i) Electron microscopic section of mouse tumor 12 hours after palladium complex treatment.

Keywords: Metallophilic interactions; Anticancer metallodrug; Photosensitizers; Cell imaging

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REWRITING CANCER IMMUNE CYCLE WITH ENGINEERED APC-LIKE NEUTROPHILS OPTIMIZING ANTIGEN PRESENTATION IN GENETIC IMMUNOTHERAPY

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Neutrophils, the most abundant immune cells, are emerging orchestrators of tumor immunity, yet their therapeutic exploitation remains limited by transient lifespan and functional plasticity. Capitalizing on the existence of rare endogenous antigen-presenting neutrophil subsets in vivo, we engineered bifunctional antigen-presenting cell (APC)-like neutrophils designed to overcome tumor immune evasion by synergizing genetic and immunotherapeutic strategies. Using CRISPR-Cas9-mediated genetic manipulation and carboxyl-mediated nanoliposome conjugation, we constructed a cellular nanoplatform surface-anchored with CFP-10 peptides. These engineered neutrophils achieve tumor-specific accumulation via self-amplifying chemotaxis while delivering PyroCas9 plasmids to induce sustained immunogenic pyroptosis. Crucially, they present both endogenous tumor antigens and exogenous peptide complexes, establishing dual immune activation: direct MHC-restricted antigen presentation bypasses conventional dendritic cell priming, while secondary antigen exposure reverses T cell exhaustion. This strategy dismantles the tumor microenvironment by simultaneously disrupting immunosuppressive barriers and reprogramming adaptive immunity. In murine models, these engineered neutrophils demonstrated superior tumor penetration and elicited durable cytotoxic lymphocyte responses, achieving an 83% improvement in survival. This first-in-class APC-mimetic neutrophil platform establishes a novel cell-gene immunotherapy paradigm by harnessing innate immune plasticity for precision cancer targeting.

A RADIOTHERAPY-RESPONSIVE PEPTIDE HYDROGEL FOR PULSATILE RELEASE OF MRNA-LNPS SYNERGIZES WITH IMMUNE ACTIVATION TO PREVENT BREAST CANCER RECURRENCE

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Introduction: Adjuvant radiotherapy (ART) is a widely used treatment after tumor resection to prevent tumor recurrence. A major limitation of ART lies in its insufficient capacity to elicit durable antitumor immunity, typically due to inadequate tumor-associated antigen supply. Although mRNA vaccines provide a promising strategy to supplement neoantigens, current delivery systems require multiple injections and lack spatiotemporal synchronization with radiotherapy, underscoring the need for more precise and adaptive platforms. Here, we first present a radiotherapy-responsive peptide hydrogel (NBS^{Gel}) that enables radiation-synchronized pulsatile release of mRNA-loaded lipid nanoparticles (mLNPs). NBS^{Gel} is formed by co-assembling two sulfide-modified peptides (NapS and BenS) with distinct oxidation sensitivities, yielding stepwise hydrogel disassembly under fractionated radiation. NBS^{Gel}@mLNP enables pulsatile mLNP release from a single dose, mimicking multi-injection vaccination while synchronizing antigen availability with DC recruitment.

Result: In postoperative tumor recurrence models, NBS^{Gel}@mLNP combined with ART markedly amplified antigen-specific $CD8^+$ T-cell responses, reduced tumor relapse by up to 80%, and prolonged survival, outperforming intramuscular vaccination and non-pulsatile controls.

Conclusion: This work proposes a pulsatile antigen release platform with γ-ray response. By using material intelligent response for radiotherapy, it achieves precise coordination between mRNA vaccine delivery after surgery and the time window for DC maturation, significantly enhancing the anti-tumor immune effect. This strategy provides a new material paradigm for immune prevention of tumor recurrence after surgery, and has good biological safety and translational potential.

A NIR Light-Driven Transformable Liquid Metal-Based Nanovaccine for Inhibiting Postoperative Colorectal Cancer Recurrence

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Key words: colorectal cancer, postoperative recurrence, liquid metal, transformable nanovaccine, immunotherapy

Abstract: Cancer vaccines induce potent immune memory responses and are highly promising for restraining postoperative colorectal cancer (CRC) recurrence. However, poor lymph node transport and antigen cross-presentation impair further clinical application of vaccines. To address these limitations, we fabricate a transformable liquid metal-based nanovaccine (LMV), which can aggregate and transform from sphere (50 nm) into fusiform sharp (500 nm) under NIR irradiation. After subcutaneous injection at tail base of mice, LMVs drain to inguinal lymph node and are subsequently internalized by dendritic cells. Giving NIR irradiation to the lymph node area, dendritic cell-internalized LMVs transform and mechanically rupture endosome membranes, which strengthens cytoplasmic delivery of LMVs and subsequent antigen cross-presentation. Meanwhile, the morphology transformation of LMVs promotes lymph node retention, resulting in continuous dendritic cell stimulation. Dual effects of LMVs significantly activate downstream cytotoxic T cells and elicit strong systemic immune response. In incomplete tumor resection model, LMVs exhibit good biosafety. Furthermore, the transformable LMV group remarkably decreases tumor volumes than PBS group and 4 out of 9 mice achieve complete healing. Especially, the cured mice in transformable LMV group almost completely inhibit liver or lung metastasis in re-challenge models, indicating potent specific immune memory. In conclusion, cancer vaccines are particularly promising “tools” to eliminate residual lesions and achieve durable remission after surgery. We prepare a controllable transformable nanovaccine, which provides a newly postoperative CRC prevention approach.

BARRIER-PENETRATING, BIOACTIVE SMALL GOLD NANOPARTICLES ENTER CHALLENGING DISEASE SITES AND ALLEVIATE CHRONIC DISEASES

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Nanoparticles are established drug carriers, but with drugs, targeting ligands, and carrier included, they become too bulky to evade liver sequestration and penetrate biological barriers to reach other disease sites upon intravenous (i.v.) injection. Previously, we discovered that i.v.-injected small gold nanoparticles (~10 nm) cross glomerular filtration and blood-brain barriers to reach fibrotic tubules and degenerative striatum, respectively, with low liver sequestration. Notably, small gold nanoparticles reduce kidney fibrosis and Huntington's disease without chemical or biological drugs. We can controllably prepare them at a 5-liter scale. Pending validation of long-term safety, small gold nanoparticles should have the translational potential of becoming barrier-crossing, bioactive therapeutics for diverse chronic diseases (often leading causes of death and disability and leading drivers of healthcare costs). Below, we illustrate our vision using two additional types of chronic diseases:
Atherosclerosis underpins stroke and myocardial infarction (both leading causes of death globally). Existing options are invasive (e.g., bypass surgery and balloon angioplasty) or only retard disease progression (e.g., statin). Delivery to plaques (whose buildup in blood vessels leads to atherosclerosis) is inefficient. Here, we prove in apolipoprotein E knockout mouse models of atherosclerosis that 11-nm gold particles fully penetrate multiple plaque tissues in the body, yet 40- and 70-nm particles merely stay beneath the endothelium; surprisingly, all three particles predominantly enter plaques via active cellular transport even though the smallest particle most favors passive entry. The 11-nm gold particle reduces plaques more effectively than the 70-nm gold particle and statin; it inhibits the fibroblast growth factor receptor on the plaque cell membrane (by kinome profiling) and lipid metabolism inside endothelial cells and macrophages (by single-cell RNA sequencing; RNA-seq). Only 5% of

the injected dose (%ID) of 11-nm gold particles remains in the liver 1-year post-treatment (as opposed to ~30 %ID for 40-nm gold particles) without systemic toxicity; such clearance is one of the most efficient for inorganic nanoparticle-based therapeutics.

Peripheral neuropathic pain is prevalent (10% globally), arisen from nerve injury and degeneration. Existing drugs cause addiction (e.g., opioid) and depression (e.g., pregabalin) or require invasive intrathecal injection. Delivery to dorsal root ganglion (DRG), a key site for pain transmission, is scarce. Here, we prove in rats with chronic constriction injury-induced pain that small gold particles cross the blood-DRG barrier and preferentially enter DRG; i.v.-injected 11-, 23-, and 60-nm gold particles all enter the injured sciatic nerve, but only the smallest particle shows enhanced deposition in the injured DRG. The 11-nm particle reduces mechanical allodynia and thermal hyperalgesia (as effectively as pregabalin), but larger gold particles do not; it activates oxidative phosphorylation and modulates axonogenesis in DRG neurons and satellite glial cells (by single-nucleus RNA-seq). Only ~3 %ID of the smallest particle remains in the liver 15-month post-treatment without systemic toxicity.

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A brush-like dual-adjuvant M13 Nanovaccine against avian influenza infection

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Keywords:
M13 phage, brush-like M2e peptide, Gold nanoparticle, Influenza virus, TLR9/NLRP3 pathway

Abstract

M2e is the extracellular polypeptide fragment of the M2 protein of various avian influenza virus strains and is highly conserved[1]. Studies have shown that antibodies against the M2e peptide can induce the body to clear virus-infected cells, thereby effectively resisting the virus[2]. However, the M2e peptide consists of only 23 amino acids and has relatively low immunogenicity. Herein, we developed a brush-like M2e peptide-functionalized dual-adjuvant M13 nanovaccine. This nanovaccine integrates the M13 phage genome, which contains CpG-rich motifs that target endosomal TLR9 and activate antigen-presenting cells (APCs) via the MyD88 signaling pathway, along with gold nanoparticles (AuNPs) engineered through site-directed mutagenesis of the PVIII protein on the M13 phage and peptide affinity coupling technology to activate the NLRP3 inflammasome. TEM and MS analysis indicated that each M13 nanovaccine was modified with approximately 93 AuNPs and 1,150 M2e peptide molecules. *In vitro* studies demonstrated the M13 nanovaccine has an exceptional biosafety and potent BMDC activation via concurrent TLR9/NLRP3 pathway stimulation, triggering elevated secretion of IL-12p40, TNF-α, IL-18, and IL-1β to orchestrate adaptive immunity. *In vivo* evaluations demonstrated that the brush-like M2e peptide-functionalized M13 nanovaccine significantly enhanced the anti-M2e antibody titer, induced potent antibody-dependent cell-mediated cytotoxicity (ADCC) activity, and promoted robust differentiation of $CD4^+$ and $CD8^+$ T cells, while increasing secretion of IL-4 and IFN-γ cytokines. Crucially, the brush-like M2e peptide-functionalized dual-adjuvant M13 nanovaccine conferred complete (100%) protection against lethal H1N1 challenge. These findings validate the feasibility of this brush-like M2e peptide nanovaccine platform as a universal subunit candidate against influenza viruses and highlight its strong potential for preventing and controlling other viral diseases in the future.

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REVERSEIBLE MANIPULATION OF THE HIERARCHICAL LIGAND ANISOTROPY FOR MACROPHAGE REGULATION

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Hierarchically structured nanomaterials with multiscale anisotropy were remotely controlled to modulate macrophage polarization. Magnetic nanomaterials (sub-microscale templates) were coated with ligand-functionalized gold nanomaterials (nanoscale) and coupled to substrates via flexible linkers. Ligand density was kept constant across isotropic/anisotropic designs. Magnetic control enabled reversible positioning to manipulate scale-specific effects.

Macrophages favored sub-microscale anisotropy for enhanced integrin clustering, promoting M2 polarization via ROCK2 signaling. Crucially, magnetic upward positioning canceled sub-microscale anisotropy benefits, while downward positioning amplified nanoscale anisotropy effects, reversing polarization trends.

This design decoupled the impact of hierarchical anisotropy scales on cell-material interactions. It demonstrates programmable immune modulation through remote material reconfiguration, offering insights for immunotherapy and tissue engineering.

MATHEMATICAL MODELING OF LIGAND NETWORKS FOR REVERSIBLE CELL RESPONSE

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The intricate ECM network in biological systems dynamically regulates cells, influencing immune responses in inflammation, bleeding, and disease development. Modulating immune cell polarization, particularly in macrophages, impacts cancer cell behavior, immune response, and evasion. Precise control of adhesion-mediated polarization is crucial in optimizing the immune response against cancer, integral to effective therapy. However, there has been no prior analysis or modeling of the complex ECM network structures within the microenvironment to optimize the immune response. In this talk, I introduce modeling an ECM-mimicking system using elongated or iron-based magnetic nanomaterials to modulate immune responses.

Firstly, I will describe the mathematical modeling of dynamic ligand network interconnectivity through selective blocking with elongated iron-based nanomaterials for anticipating cell-materials interactions both in vitro and in vivo. Dynamic control of ligand interconnectivity based on mathematical modelling enables the modulation of macrophage adhesion-mediated polarization phenotype. This approach holds promise for furthering our comprehension of ECM functionality including immune response and its potential applications in diverse biological contexts.

Lastly, I will also illustrate a couple of recent cancer therapies with models utilizing one-dimensional nanomaterials or Fenton-reaction-based ferroptosis employing iron ions. Developing materials tailored for precise and effective cancer treatment, as exemplified by diverse application cases, paves the way for patient-specific, non-invasive therapies in the future. This approach holds the potential to mitigate the side effects associated with current treatment modalities while enhancing overall treatment efficacy.

SUBMOLECULAR-LEVEL DYNAMIC ENGINEERING OF LIGAND NANOSTRUCTURE FOR MACROPHAGE IMMUNOREGULATION

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Receptor–ligand interactions at the cell–material interface critically regulate macrophage adhesion, polarization, and overall immune behavior. In the extracellular matrix, adhesive proteins, such as RGD motifs, experience nanoscale stretching and compression during integrin binding. These dynamic conformational changes occur within the submolecular regime—comparable to the integrin's size—making the structural availability of ligands a key factor in guiding macrophage function.

In this work, we present a series of strategies to dynamically engineered ligand nanostructure and availability at the submolecular level to direct macrophage immunoregulation. These nanobiomaterials are designed to reversibly control ligand accessibility using external magnetic or photonic stimuli.

First, we introduce magnetically responsive nanoaggregates tethered above liganded surfaces. These aggregates can be magnetically lifted or lowered to reversibly block or expose the underlying ligands. This enables real-time switching of receptor–ligand interactions, allowing precise control over macrophage adhesion and activation.

Second, we engineer ligand size and spacing at sub-integrin resolution through template-mediated ligand growth and magnetic anchoring. By tuning these nanoscale parameters, we show that macrophage adhesion, spreading, and phenotypic polarization can be significantly modulated, highlighting the functional relevance of spatial ligand design.

Together, these approaches demonstrate a versatile platform for remote, reversible, and programmable control over interactions between immune cells and nanobiomaterials at the submolecular scale. By integrating dynamic materials, hierarchical self-assembly, and physical stimuli, this work opens new avenues for immunomodulation in applications such as cancer immunotherapy, inflammation control, and development of smart nanobiomaterials.

VERSATILE ENGINEERING OF LIGAND SPACING ON SELF-ASSEMBLY TO REGULATE STEM CELL DIFFERENTIATION

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Self-assembly dynamically responds to external stimuli by regulating biochemical reactions of monomers for in situ modulation of morphology and functions. Stem cell fate is determined by interacting with submolecular spacing of ligands in the supramolecular structures of cellular microenvironment. However, ligand spacing on the biomaterial surface and its dynamic control at the submolecular level in vivo has not been reported. To this end, I will introduce the unique design of dynamic supramolecular and supra-particle nanomaterials that can be remotely controlled by tissue-penetrative signals, including magnetic field and light.

First, I will present liganded supra-particle nanoassembly with tunable local ligand spacing on magnetic nanoparticles while keeping macroscale ligand density constant. Decreasing ligand spacing under cell-adhesive integrin diameter as well as falling liganded nanoassembly promotes stem cell adhesion-mediated osteogenic differentiation. Next, I will show photoreversible supramolecular liganded self-assembly of cationic azobenzene and liganded polyanions formed via cation-π and electrostatic interactions. Depending on the irradiated light wavelength, the self-assembly can deflate and inflate to reduce or increase ligand spacing in submolecular scale, respectively, to regulate stem cell differentiation.

I will also illustrate approach to future design of in situ self-assembly for effective biomedical application. In situ self-assembly constructed by the monomers reactive to endogenous and exogenous stimuli can provide unprecedented opportunities for targeted and efficient patient-specific therapies and diagnoses while minimizing side effects from traditional approaches.

Keywords: self-assembly, regenerative therapy, submolecular ligand spacing

DYNAMIC CONTROL OF LIGANDED NANOGEOMETRY FOR CELLULAR REULGATION

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Cellular behavior is profoundly influenced by the nanoscale geometry and biochemical presentation of surrounding materials, especially when these features can be dynamically modulated. In regenerative medicine and cancer therapy, remotely controllable nanomaterials provide powerful means to emulate complex biophysical environments and regulate cellular responses. However, reproducing the coordinated distribution of ligands and mechanical forces found in native tissues remains a major challenge in biomaterial design.

To address this, magnetically controllable nanoassemblies and nanogroove platforms were developed to examine how nanoscale geometry and dynamic ligand presentation affect stem cell behavior. Spherical nanoassemblies (200–700 nm) with ligands under magnetic control showed size-dependent effects: smaller assemblies promoted integrin clustering and osteogenic signaling, while larger ones suppressed these responses. Similarly, nanogroove templates composed of liganded magnetic nanoparticles demonstrated geometry-dependent adhesion. Grooves with widths of 50 nm, 80 nm, and 110 nm showed distinct outcomes: small grooves restricted filopodial access, large grooves provided constant adhesion, and medium grooves exhibited switch-like behavior where magnetic lifting exposed ligands and activated osteogenic differentiation. These findings highlight the importance of precisely controlled nanoscale ligand presentation and dynamic mechanical modulation in directing cell fate.

Geometry specific nanomaterials also show distinct physical behaviors such as movement, heat generation, and mechanical actuation under external fields, influencing therapeutic performance and enabling strategies to overcome drug resistance. Together, these results underscore the potential of stimuli responsive, geometry tailored nanomaterials for spatiotemporal regulation of cell behavior, advancing the development of biomimetic systems for regenerative medicine and precision oncology.

Graph theory-based mathematical modeling of nanoligand networks regulating reversible stem cell fate

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The extracellular matrix (ECM) is an interconnected nanoscale network that regulates stem cell adhesion, mechanosensing, and differentiation. However, systems enabling reversible and quantitative control of ligand inter-cluster connectivity have been lacking.

This study introduces a graph theory–based modeling and magnetic control platform for tuning the connectivity of gold nanoparticle (GNP)-based ECM-mimetic ligand networks. Using anisotropic magnetic nano-blockers, ligand interconnections were selectively disrupted without changing ligand density or spacing. Delaunay triangulation and Louvain clustering quantified inter-cluster edges as a metric of nanoscale connectivity.

Higher blocker anisotropy reduced inter-cluster edges and stem cell mechanotransduction (integrin β1, focal adhesion, YAP/RUNX2), while magnetic field–induced cyclic elevation of blockers restored connectivity and cellular responses.

In vivo, cyclic magnetic actuation enhanced stem cell adhesion, focal adhesion formation, and nuclear YAP/RUNX2 localization without toxicity.

Overall, this work demonstrates reversible, non-invasive regulation of cell–material interactions through nanoscale ligand connectivity, providing a predictive strategy for dynamic, ECM-like biomaterials applicable to regenerative medicine and tissue engineering.

Liver-Targeting mRNA Vaccine Ameliorates Pollen Allergy by Enhancing Regulatory T Cell Induction

Pollen allergy is a leading contributor to respiratory allergic diseases, characterized by increasing prevalence and chronic severity. Although allergy immunotherapy (AIT) can modify disease progression, its efficacy is limited by inefficient allergen delivery and inadequate induction of regulatory T cells (Tregs). Here, we developed a liver-targeted mRNA vaccine using mannose-decorated lipid nanoparticles (LNP-mArt v 1) to deliver a T cell epitope of the pollen allergen Art v 1. This platform promoted immune tolerance by upregulating IL-10 and TGF-β1 expression in the liver. In both therapeutic and prophylactic murine models of pollen allergy, LNP-mArt v 1 significantly alleviated allergic symptoms and enhanced Treg and T helper type 1 immune responses. Mechanistic studies further revealed that LNP-mArt v 1 specifically induced upregulation of regulatory T and B cells, unlike protein-based vaccines. These findings highlight the potential of liver-targeted mRNA delivery as a next-generation AIT strategy for pollen allergies through robust immune tolerance.

GLYCOCONJUGATE PRODUCTION IN LIPOSOMES

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Liposomes are widely used as clinically approved drug carriers to treat cancer, fungal and viral infections. To date, translational studies using liposomes have been limited to delivery systems alone. This project aims to utilise liposomes for *in vitro* production and expression of glycoconjugate vaccines. Glycoconjugates are composed of polysaccharides covalently attached to a carrier protein. Currently, three methods exist for glycoconjugate production – chemical conjugation, click chemistry and bioconjugation – which are limited by high costs, and for the latter, low yield. Recent advances in synthetic biology offer an alternative approach for rapid and scalable glycoconjugate production by using liposomes (lipid vesicles) and *in vitro* transcription and translation (IVTT). Herein plasmids with two meningococcal proteins – HpuA and fHbp, and one pneumococcal protein – PiuA, with a N–terminal fluorescent tag under an IPTG inducible promoter were constructed using ligation–independent cloning. SDS–PAGE demonstrated that fusion protein expression via IVTT was successful. Similar observation was seen in *E. coli* strains with the plasmid of interest five–hour post–induction. Currently, encapsulation of IVTT machineries for bacterial vaccine antigen production and expression in liposome is underway with ongoing work focusing on multiple protein expression and glycan conjugation with carrier protein inside liposomes and display of resulting glycoconjugate on liposomal surface. In doing so, this study will pave way to synthesizing cost–effective and rapid response glycoconjugates against mucosal bacterial threats by bypassing purification of the protein–glycan complex.

GRADIENT HYDROGEL–NANOFIBER NERVE GUIDANCE CONDUIT WITH MULTIPLE INDUCTIVE CUES PROMOTES PERIPHERAL NERVE REPAIR IN PRIMATE MODELS

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Peripheral nerve injury (PNI) is a common clinical condition that causes severe sensory and motor dysfunction. Although autografts remain the clinical gold standard, their application is limited by donor scarcity and mismatched nerve dimensions, which has led to the development of nerve guidance conduits (NGCs) as promising alternatives. We designed and fabricated aligned fibrous scaffolds using electrospinning and electrospraying techniques, in which bioactive particles were loaded with a gradient density to promote axonal extension and nerve regeneration. On this basis, we further addressed the critical challenge of coordinating multiple inductive signals in space and time to efficiently guide nerve regeneration. In this study, we developed a gradient-structured NGC composed of electrospun aligned nanofibers, electrosprayed bioactive particles, and hydrogels with a crosslinking-density gradient, designed to integrate topographical, chemotactic, haptotactic, and stiffness cues along the proximal-to-distal axis. This structure enabled ordered degradation and sustained bioactive factor release. The conduit promoted Schwann cell migration, axonal elongation, and vascularized nerve formation in vitro. In a 10 mm rat sciatic nerve defect model, regenerated nerves showed electrophysiological recovery, myelination, and muscle reinnervation comparable to those of autografts. Furthermore, in a 30 mm median nerve defect model in rhesus monkeys, the conduit supported organized axonal regeneration with minimal connective tissue formation, while functional recovery after six months was equivalent to autograft repair. Transcriptomic analysis revealed the regulation of genes associated with angiogenesis, cell migration, and myelination. These results demonstrate that the gradient-structured, photothermal-responsive NGC effectively promotes long-gap nerve regeneration and provides a feasible alternative for clinical peripheral nerve repair.

Keywords: electrospinning; nanofibers; hydrogel; peripheral nerve repair

REDOX-DISRUPTED DISELENIDE POLYMERSOMES FOR TUNABLE ORGANELLE TARGETING AND THERAPEUTIC SYNERGY

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Precise control of intracellular drug localization and redox modulation is essential for enhancing therapeutic outcomes. This study presents a redox-disrupted diselenide polymersome platform, called PSe_2-NP, which facilitates organelle-specific delivery and coordinated redox imbalance. The system was made from a diselenide-bridged amphiphilic polymer capable of separately loading either hydrophilic doxorubicin hydrochloride (HP) or hydrophobic doxorubicin free base (HB). Two doxorubicin derivatives, identical in backbone but differing in hydrophilicity or hydrophobicity, were individually encapsulated to produce HP@PSe_2-NP and HB@PSe_2-NP. These polymersomes remained stable in water but underwent reduction-driven bond cleavage inside cells. Breaking Se-Se bonds caused different patterns of payload release. Despite this, diselenide cleavage depleted glutathione and increased reactive oxygen species, generating self-amplifying ROS. HP@PSe_2-NP targeted both the nucleus and mitochondria by combining redox-induced oxidative stress with nuclear DNA intercalation, while HB@PSe_2-NP selectively accumulated in mitochondria, disrupting electron transport and increasing oxidative damage. Both formulations exhibited potent cytotoxicity and significant tumor growth inhibition, while remaining safe systemically in vivo. These findings demonstrate that selectively loading hydrophilic or hydrophobic drugs into diselenide polymersomes enables synergistic, programmable redox therapy, establishing a comprehensive framework linking redox imbalance with organelle-specific precision in cancer treatment.

SYNTHESIS AND CHARACTERIZATION OF PORPHYRIN-BASED NANOMATERIALS FOR CATALYTIC CANCER THERAPY

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Nanomaterials with enzyme-like activities have emerged as a powerful platform for artificial enzyme technology, owing to their low cost, high stability, tunable catalytic performance, and scalable production. Among their biomedical applications, these catalytic nanomaterials hold significant potential for cancer therapy by converting endogenous substrates within the tumor microenvironment into reactive oxygen species (ROS), enabling oxidative injury to tumor cells without the need for external energy input. However, their clinical translation remains limited by harsh synthesis conditions (*e.g.*, high temperatures, multistep processes), insufficient ROS generation, and low catalytic efficiency. Here, we report porphyrin-based catalytic nanomaterials (POZYs), synthesized under simple, mild conditions, that simultaneously activate multiple catalytic pathways to amplify ROS generation.

The resulting POZYs formed spherical nanoparticles with a size of ~120 nm (TEM) and a hydrodynamic diameter of ~200 nm (DLS), and exhibited excellent colloidal stability (polydispersity index ~0.13; ζ potential ~−32 mV) in both phosphate-buffered saline and cell culture media. Functionally, POZYs demonstrated robust multienzyme-mimetic activities, including peroxidase (POD), catalase (CAT), and oxidase (OXD)–like functions. These synergistic activities enabled the direct catalytic conversion of endogenous H_2O_2 and O_2 into cytotoxic hydroxyl radicals ($^{\bullet}OH$) and superoxide anions ($O_2^{\bullet-}$) under tumor-relevant conditions. Kinetic analysis confirmed favorable catalytic performance, with V_{max} and K_m values of 5.3×10^{-8} M s^{-1} and 22.7 mM for POD-like activity, and 2.9×10^{-8} M s^{-1} and 1.2 mM for OXD-like activity, respectively.

With their strong catalytic efficiency and enhanced multi-ROS generation, POZYs represent a promising nanomedicine platform for further *in vitro* and *in vivo* evaluation in catalytic cancer therapy.

Chemoimmunological Intervention of Crosstalk between Tumor Microenvironment and Draining Lymph Node for Improved Cancer Immunotherapy

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Cancer immunotherapy has demonstrated significant potential as a cancer treatment by enhancing the immune system's ability to recognize and eliminate cancer cells. However, its efficacy can be limited by factors such as tumor heterogeneity, immunosuppressive tumor microenvironments, and systemic toxicities. Recent advances in drug delivery systems have facilitated the development of more targeted and personalized cancer therapies. Microneedles have emerged as a promising platform for non-invasive and highly localized drug delivery, directly administering drugs, vaccines, and other therapeutic agents to the skin. In this study, we designed dissolving microneedles (dMN) based on a biocompatible amphiphilic tri-block copolymer, which enables the self-assembly of nano-micelles containing hydrophobic drugs when applied to the skin. We used the dMN technology to formulate SKKU-06, a hydrophobic natural immune modulator toxin derived from fungi, which exhibits anti-cancer and immunomodulatory properties in melanoma (SSKU-06@dMN). After intratumoral application of SSKU-06@dMN to skin tumors, the drug-loaded nano-micelles can migrate to tumor-draining lymph nodes (TDLN). The dMN-guided delivery of SKKU-06 to skin tumors and TDLN induced immunogenic cell death and stimulated the activation and maturation of antigen-presenting cells (APCs), promoting the development of humoral and cellular anti-tumor immunity. Furthermore, the immunomodulatory effects of SSKU-06@dMN were enhanced when combined with anti-PD-1 treatment, impacting the tumor microenvironment through increased intratumoral CD8+ T cell infiltration and reduced Treg populations. This resulted in efficient growth inhibition of established skin cancer and metastatic cancer, as well as prolonged survival. The dMN-guided lymphatic delivery of SKKU-06 demonstrates potential for treating metastatic solid tumors and improving cancer immunotherapy efficacy by modulating the tumor microenvironment.

DUAL-PATHWAY STING NANO-AGONIST FEATURING IMMUNOSUPPRESSIVE MICROENVIRONMENT REPROGRAMMING FOR HEPATOCELLULAR CARCINOMA THERAPY

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The cyclic GMP-AMP synthase-stimulator of interferon genes (cGAS-STING) pathway, a critical axis in innate immunity, has emerged as a promising immunotherapeutic target for hepatocellular carcinoma (HCC). Nevertheless, due to the poor stability, inefficient intracellular delivery, and rapid proteasome-mediated degradation of activated STING following its endoplasmic reticulum (ER)-to-Golgi apparatus trafficking, the conventional nucleotide-based STING can only achieve clinical efficacy as resulted from insufficient transient and immune activation. Through engineering sulfobutyl-β-cyclodextrin (SCD)-encapsulated artesunate (Art), manganese ions (Mn^{2+}), and glycyrrhetinic acid (GA)-functionalized liposomes, we developed a dual-targeting STING nanoagonist (Mn^{2+}-SCD/Art@LP-GA) which can sustain and amplify STING signaling via coordinated upstream activation and downstream stabilization mechanisms. Via a fenton-like reaction, Mn^{2+} can catalyze Art-driven reactive oxygen species (ROS) generation for oxidative DNA damage. The released cytosolic DNA can synergize with Mn^{2+} (one cGAS cofactor) to enhance cGAS activity and cyclic GMP-AMP (cGAMP)-STING binding affinity, effectively amplifying upstream cGAS-STING activation. Also, SCD-mediated Golgi targeting can promote STING oligomerization and sustained the TANK-binding kinase 1 (TBK1)-interferon regulatory factor 3 (IRF3) phosphorylation cascade while counteracting STING proteasomal degradation and prolonging interferon-beta (IFN-β) secretion, thereby stabilizing downstream cGAS-STING signaling. The amplified and sustained cGAS-STING pathway activation can further promote dendritic cell maturation and cytotoxic $CD8^+$ T-cell infiltration, collectively enhancing systemic antitumor immunity. This study presents a rationally designed nanoagonist has the potential to full unlock the therapeutic potential of the cGAS-STING axis for improving the precision immunotherapy for HCC.

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A SKIN-COMPATIBLE AND PHOTOTHERMALLY-ACTIVATED ELECTRONIC TATTOO FOR DEPTH-TUNABLE TRANSDERMAL DRUG DELIVERY

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Transdermal drug delivery (TDD) is painless and patient-friendly but is restricted by the stratum corneum. The present study demonstrates an ultrathin, flexible, and breathable multi-drug-loaded electronic tattoo (MDET) that enables light-triggered and depth-tunable transport of both hydrophilic and hydrophobic drugs. A key factor is the amphiphilic silk-fibroin (SF) reservoir: its hydrophilic segments and hydrophobic β-sheet domains provide dual affinity, and mild crosslinking yields a water-insoluble, nanostructured matrix that co-loads dissimilar drugs with no surfactant, and enables photothermally responsive release. Structurally, the MDET combines a porous cellulose nanofiber scaffold for breathability with a graphene layer for photothermal heating; the MDET maintains a stable electrical performance, excellent skin conformability, and high moisture permeability, while maintaining strong skin-adhesion. Under the gentle 617 nm LED illumination, graphene rapidly converts light to heat and transiently loosens the stratum corneum for efficient drug transport. Using 1 mM rhodamine B (RB) as a tracer, penetration increased from 85 ± 15 µm at 2 min to 456 ± 25 µm under the 10-min-illumination, with >50% of the initial load released to the skin surface. In addition, macromolecular delivery was likewise programmable: rhodamine–dextran (10 kDa) advanced from 55 ± 22 µm to 176 ± 18 µm (2–10 min) and reached the dermis, whereas 70 kDa dextran crossed the barrier but remained largely within the epidermis (~30 ± 8 µm to ~110 ± 10 µm), evidencing layer-specific control by tuning molecular weight. Consistent with SF's dual-affinity reservoir, the MDET simultaneously delivered drugs with diverse wetting properties (RB and Quercetin). In an artificial skin model, light-activated MDET patches loaded with arbutin, nicotinamide, and kojic acid reduced melanin to ~45%, outperforming unilluminated controls; biocompatibility assays showed 95.9% tissue viability, classifying the device as non-irritant. Overall, this skin-conformal platform integrates gentle photothermal activation with an amphiphilic silk reservoir to achieve on-demand, multi-class TDD with tunable depth from epidermis to dermis, advancing practical, personalized dermatologic and cosmetic applications.

Title: Engineered Immunotherapies for Precise Disease Management

Speaker Introduction: Dr. Yun CHANG is an Assistant Professor in the Department of Biomedical Engineering at The Hong Kong Polytechnic University. He earned his Bachelor's degree from Jilin University in 2013 and his Ph.D. from the Changchun Institute of Applied Chemistry, Chinese Academy of Sciences in 2019. Following his doctoral studies, he conducted postdoctoral research at Purdue University, USA (2019-2024). In 2024, he joined The Hong Kong Polytechnic University as an Assistant Professor and received the PolyU President's Young Scholar Fund. His primary research focuses on gene editing, directed differentiation of human pluripotent stem cells, and the application of intelligent, functional biomaterials in immunotherapy for diseases. He has authored or co-authored over 40 SCI-indexed papers as first or corresponding author in journals including Nature Communications, Bioactive Materials, Advanced Materials, Nano Letters, Advanced Science, Nano Today, Biomaterials, Cell Reports, ACS Applied Materials & Interfaces, and Nano Research, and holds 6 patents.

Lecture Abstract: Glioblastoma (GBM) is one of the most aggressive and lethal solid tumors in humans. Despite advances in cancer therapies, including chimeric antigen receptor (CAR) T cells and chemotherapeutics, their efficacy against GBM remains limited due to the blood-brain barrier. Human neutrophils can naturally cross physiological barriers and exhibit strong immune responses against pathogens. However, their short lifespan and resistance to genome editing have restricted their broad application in immunotherapy. To address these challenges, we genetically engineered human pluripotent stem cells (hPSCs) to express synthetic CARs and differentiated them into functional neutrophils via a chemically defined platform. These CAR-neutrophils demonstrated potent and specific cytotoxicity against tumor cells in both in vitro and in vivo models. Furthermore, the most potent CAR-neutrophils were engineered for non-invasive delivery of tumor-microenvironment-responsive nanomedicines, effectively targeting GBM without inducing additional inflammation at the tumor site. We also explored the synergistic anti-tumor effects of CAR-neutrophils and CAR-NK cells, where neutrophils modulate the tumor microenvironment while NK cells provide targeted cytotoxicity. To enhance therapeutic applicability, we developed a Neutrophil-Specific modRNA Translation (NeuSMRT) system, enabling successful delivery of modRNA-encoded CAR constructs to primary neutrophils both in vitro and in vivo. This innovative approach offers a promising strategy to overcome therapeutic barriers in GBM and advance immunotherapy.

A Human Stem Cell-based 3D Microphysiological Platform for Skeletal Muscle Disease Modeling and Therapeutic Discovery

The development of effective therapies for muscle-wasting disorders like sarcopenia and Duchenne Muscular Dystrophy (DMD) is hampered by the poor predictive power of traditional 2D cell cultures and animal models. To address this, we have established a novel human-based 3D skeletal muscle (3DSM) platform for high-fidelity disease modeling and drug screening.

Our platform involves differentiating human pluripotent stem cells into myogenic progenitor cells, which are then embedded in a hydrogel within a custom micro-bioreactor. This system supports the self-organization of functional 3D muscle tissue exhibiting aligned myotubes, expression of muscle-specific proteins, and measurable contractile force upon electrical stimulation. We successfully modeled muscle atrophy in vitro by introducing pathophysiological stressors, such as hydrogen peroxide (H2O2) and inflammatory cytokines (TNF-α), which resulted in characteristic hallmarks of disease including reduced cell viability, impaired myotube formation, and a significant decrease in force production. Furthermore, we validated the platform's utility for therapeutic discovery by demonstrating that treatment with Enobosarm, a selective androgen receptor modulator, significantly rescued muscle function post-injury.

This human-relevant, high-throughput platform bridges a critical gap between conventional models and human physiology. It serves as a powerful New Approach Methodology (NAM) for de-risking drug candidates, quantifying functional and phenotypic metrics, and accelerating the development of therapies for debilitating muscle diseases.

MULTI-TARGETING OF INJURED ROTATOR CUFF MUSCLE-TENDON UNITS WITH FIT MUSCLE-TENDON GRAFT

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Severe chronic diseases and musculoskeletal injuries produce a myriad of pathologies that require a multipronged treatment strategy. These sequelae, which include tissue loss, fatty degeneration, and fibrosis, are present across a spectrum of conditions ranging from rotator cuff tears and myocardial infarction to nonalcoholic fatty liver disease. Developing a single therapeutic or drug cocktail capable of targeting both regeneration and pathological degeneration is challenging. This is because the drug(s) must attain therapeutically effective and non-toxic levels within targeted cell types that are located across potentially different sites. For large-to-massive rotator cuff tears, this requires multi-targeting of tendon stem/progenitor cells, muscle stem/progenitor cells, and fibroadipogenic progenitors (FAPs) within the muscle-tendon unit to promote tenogenesis and myogenesis whilst reducing excessive myofibroblast conversion and adipogenesis. To address this challenge, we developed a drug cocktail termed FIT to achieve multi-tissue muscle-tendon regeneration while simultaneously suppressing undesired fatty degeneration for severe rotator cuff injury. First, FIT cocktail was characterized, using different in vitro conditions to mimic differentiation, fatty degeneration, and fibrosis. FIT supplementation promoted tenocyte and myotube formation while suppressing adipogenic and fibrotic lineages in human and mouse musculoskeletal cells. Next, single-cell RNA-seq revealed the cellular dynamics and signaling networks underlying FIT's mechanism-of-action in myoblasts and FAPs, which were validated by transdifferentiation and apoptosis assays. Subsequently, a muscle-tendon graft was developed and release profile of FIT was characterized ex vivo. Lastly, using a chronic-like rabbit rotator cuff injury model, implantation of muscle-tendon graft containing FIT promoted muscle-tendon regeneration and restored native contractile force whilst reducing fibrosis and fatty degeneration. Altogether, this work established a paradigm for using multi-acting drug cocktails to achieve precision multi-tissue regeneration and reduction of undesired pathology, which shows broad promise for rotator cuff tears and other chronic diseases.

PRECISION ROBOTIC FABRICATION OF ANTI-FIBROTIC BIOINTERFACES FOR MAXILLOFACIAL IMPLANT INTEGRATION

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The clinical translation of anti-fibrotic bioadhesives for implant integration faces a critical barrier: the precise surgical application in confined anatomical sites. Manual deposition is operator-dependent and often yields inconsistent coverage, compromising interface integrity and leading to fibrous encapsulation.

We developed an injectable bioadhesive (STAM) from silk fibroin methacryloyl, acrylic acid N-succinimidyl ester, tannic acid and magnesium oxide, specifically engineered for robotic compatibility. Material characterization confirmed successful synthesis, minimal swelling (near-zero swelling ratio), excellent surface wettability, and smooth injectability with low injection pressure (<2 N through 16G needle). STAM demonstrated exceptional adhesion strength on native bone (223.3 ± 65.6 kPa in lap-shear tests), 3.13 to 10.86 times greater ($p < 0.01$) significantly outperforming commercial controls COSEAL (Baxter, USA). The adhesive maintained stable adhesion for over 96 hours across various implant surfaces, including metal, biocomposite, and PEEK, while supporting excellent cell viability (>80%) and enhancing osteogenic differentiation.

Complementing this material advance, we integrated a 6-DOF robotic arm with an intraoral scanner to establish a precision deposition platform. In cadaveric mandibular models, the system achieved submillimeter deposition accuracy, enabling complete peri-implant interface coverage in complex defects. This robotic fabrication approach ensures reproducible biointerface formation, overcoming the limitations of manual application.

Our work establishes a transformative platform that bridges innovative adhesive biomaterials with robotic fabrication to address the critical challenge of implant-associated fibrosis. By ensuring precise, consistent application of anti-fibrotic bioadhesives, this technology represents a significant step toward predictable implant integration and longevity, demonstrating substantial potential for clinical translation in personalized regenerative therapy.

Chiral Nanoparticles Drive Enantiomer-specific Osteogenesis and Accelerate Stem Cell-based Bone Regeneration

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Introduction: Precise regulation of stem cell differentiation is vital for advancing regenerative medicine, particularly in bone repair. Chiral nanoparticles (NPs) have emerged as promising modulators of cellular fate due to their enantioselective (chirality-/handedness-dependent) interactions with biological systems[1,2]. However, the mechanisms by which nanoscale structural (rather than molecular) chirality directs osteogenic differentiation remain unclear.

Methods: (1) *Chiral NPs Synthesis & Characterization*: Three types of NPs with controlled structural chirality, including left-handed (L-NPs), right-handed (D-NPs), and achiral racemic (A-NPs, no chirality) NPs, were synthesized using a 2-step method. The physicochemical properties of the NPs were characterized via circular dichroism (CD), SEM, and TEM (Fig. 1A and Fig. 2A-D). (2) *In Vitro Studies*: human bone marrow-derived mesenchymal stem cells (MSCs) were treated with each NP type. Cellular uptake mechanisms were explored using Nano-CT and microscale thermophoresis (Fig. 2E-G), and osteogenic/angiogenic marker expression was quantified by qPCR and Western blot. (3) *In Vivo Tests*: Critical-sized bone defects (CSBDs, 3 mm) in femora were created in 12-week-old male Sprague-Dawley rats (n = 4/group) and treated with 3D volumetric printed scaffolds containing each NP type (Fig. 1B, C). Male rats were selected to avoid estrogen-mediated metabolic variability. Bone regeneration was assessed via micro-CT and histological analyses. Statistical analysis: Data are presented as mean ± SD. Multi-group comparisons: one-way ANOVA + Tukey's test (GraphPad Prism 10; n ≥3 biological replicates for all tests). Ethics: The animal experiments were authorized by the Animal Experimental Committee of the Seyotin (Guangdong) Co., Ltd (Approval SYT2024130).

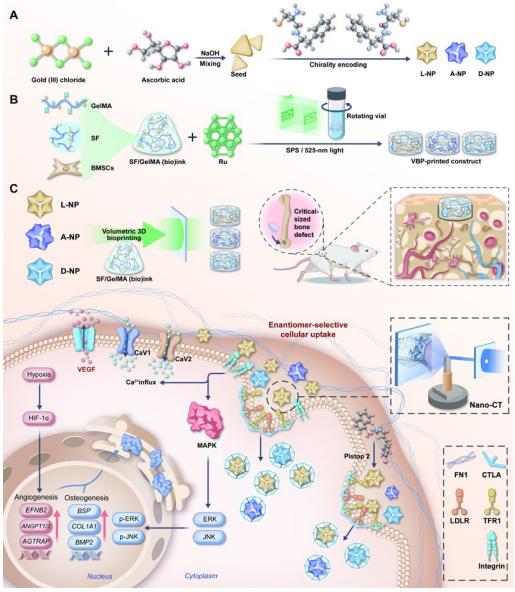

Fig. 1. Schematic of study design. (A) Diagram of chiral NP synthesis. (B) Volumetric bioprinting of NP-containing hydrogel scaffolds. (C) Mechanisms for chiral NP uptake by MSCs and associated osteogenic differentiation.

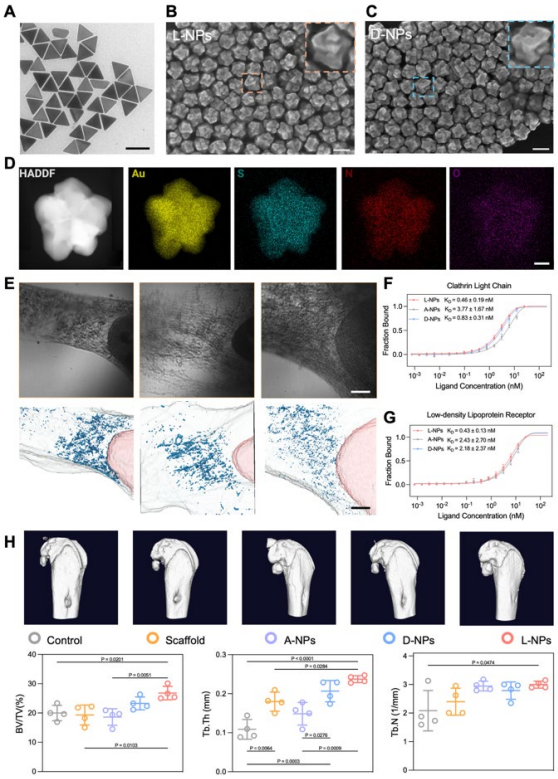

Fig.2 Chiral NP evaluation. (A) TEM image of NP seeds. (B) SEM images of L-NPs and (C) D-NPs. Scale bar = 100 nm. (D) HAADF-STEM image of L-NPs. Scale bar = 20 nm. (E) Nano-CT images of MSCs after being cultured with NPs. Scale bar = 2μm. (F, G) Binding affinity of NPs to proteins. (H) 3D reconstructed micro-CT images after 8 weeks of scaffold implantation and quantitative analysis.

Results: *In vitro*, L-NPs showed significantly higher uptake by MSCs than D-NPs and A-NPs, primarily through clathrin-mediated, integrin-associated endocytosis. This led to upregulation of osteogenic markers, increased mineral deposition, and enhanced MAPK/JNK/ERK signaling. *In vivo*, scaffolds with L-NPs resulted in the fastest bone regeneration, as evidenced by the greatest bone volume and most robust tissue integration (Fig. 2H).

Conclusions: Our results demonstrate that nanoscale structural chirality critically influences stem cell behavior, with L-NPs providing superior osteoinductive effects. The enantioselective cellular uptake and signaling activation underscore the importance of chirality as an important design parameter for regenerative biomaterials.

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MAGNETICALLY SWITCHABLE NANOSCALE GROOVE-RIDGE BIOINTERFACES FOR DYNAMIC STEM CELL REGULATION AND TRANSLATIONAL BONE REGENERATION

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Remotely actuated biomaterials that can modulate cell-matrix interactions in real time are emerging as powerful tools for regenerative medicine. However, it remains challenging to engineer clinically relevant platforms that both recapitulate the dynamic remodeling of nanoscale groove-ridge structures in native extracellular matrices and provide on-demand control over ligand accessibility, particularly in vivo.

Here, we present a magnetically switchable nanoscale groove-ridge biointerface that enables reversible control of RGD ligand presentation consists of silica nanogroove templates with groove widths of 50, 80, and 110 nm, onto which RGD-presenting magnetically activatable nanoridges are tethered via flexible PED linkers at constant ligand density. In the “groove” state, ligand-bearing nanoridges are sterically buried within the nanogrooves; upon application of an external magnetic field, they are lifted into a “ridge” state that exposes RGDs above the surface. The intermediate 80 nm structure, closely matching filopodial dimensions, shows the greatest magnetically induced increase in ligand accessibility, leading to maximal on/off differences in integrin recruitment, focal adhesion maturation, mechanosensitive signaling, and osteogenic differentiation of human mesenchymal stem cells.

Cyclic switching between hidden and exposed ligand states enables temporal programming of stem cell adhesion and osteogenesis in vitro, while subcutaneous implantation demonstrates magnetically controlled osteogenic differentiation of transplanted human mesenchymal stem cells in vivo without detectable local or systemic toxicity. This work introduces a dynamic, remotely controllable biointerface that bridges static nanotopographies and responsive therapeutic scaffolds, and highlights a translational strategy for externally controllable bone-regenerative materials. By coupling clinically compatible magnetic actuation with filopodia-scale ligand engineering, this platform provides a versatile framework for future stimuli-responsive biomaterials aimed at treating aging-, injury-, and stress-related bone defects.

PIEZO-ANCHORED HYDROGELS FOR NEURAL STEM CELL DELIVERY AND BRAIN INJURY REPAIR

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Hydrogels are widely used for stem cell delivery in brain repair, as they can enhance cell retention and survival post-implantation. However, they cannot actively generate physiologically relevant electroactive signals for inducing neuronal differentiation of stem cells and neural regeneration. Piezoelectric hydrogels can overcome this limitation through integrating the piezoelectricity (generating electric charges in response to mechanical stress or ultrasound) with hydrogels to mimic endogenous bioelectrical microenvironments. Yet, piezoelectric materials (*e.g.*, $BaTiO_3$, PZT, and PVDF) generally exhibit intrinsic rigidity and bioprocessing incompatibility, preventing their direct fabrication into hydrogel format. Currently, the dominant strategy for fabrication of piezoelectric hydrogels is simply embedding the piezoelectric nanoparticles within hydrogel networks. However, when this type of piezoelectric hydrogel was used for delivery of stem cells, we identified a critical barrier: stem cells rapidly internalize the embedded piezoelectric nanoparticles via endocytosis. This prevents the essential electrical stimulation of cell membrane voltage-gated receptors (e.g., Ca^{2+} channels) by the piezoelectric hydrogels, thereby hindering the guided neuronal differentiation and neurodevelopment.

To address this challenge, we propose to create a new type of piezoelectric hydrogel through chemically anchoring piezoelectric nanoparticles to the hydrogel network. This hydrogel, named Piezo-Anchored Hydrogel, is fabricated through pre-linking the UiO-66 piezoelectric nanoparticles to the GelMA precursor, followed by photo-crosslinking. Unlike simply embedding the piezoelectric nanoparticles within hydrogel, this Piezo-Anchored Hydrogel prevents the piezoelectric nanoparticles from being endocytosed by stem cells due to their stable anchoring to the hydrogel network while keeping the nanoparticles attached to the stem cell membrane. In this Piezo-Anchored Hydrogel, the piezoelectric nanoparticles can effectively activate the voltage-gated Ca^{2+} channels via piezoelectric stimulation under ultrasound, enhancing 43.4% of neural stem cells to differentiate into neurons within 10 days—significantly higher than the 14.5% in traditional piezoelectric hydrogels. The Piezo-Anchored Hydrogel microspheres containing stem cells can improve motor and cognitive functions of traumatic brain injury mouse models under ultrasound treatment, holding great potential in tissue repair.

FROM MONOLAYERS TO MULTILAYERS: FARADAY WAVE BIOASSEMBLY FOR ADVANCED OSTEOCHONDRAL TISSUE ENGINEERING

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Faraday wave bioassembly is emerging as an innovative biofabrication technology, demonstrating unique technical advantages and significant application potential in the engineering construction of tissues and organs. However, the inherent characteristics of potential energy distribution within the assembly medium currently restrict Faraday wave-based bioassembly techniques to a single assembly process at the bottom of the chamber, leading to the creation of monolayered patterned structures. To address this limitation, this study proposes two innovative strategies for multilayer assembly via Faraday waves: the first involves layer-by-layer patterned assembly facilitated by an “in-situ layer-by-layer superposition chamber”, while the second enables multilayer assembly with conrolled interlayer spacing through an “oil-phase-assisted filling method”. This approach is supported by mathematical models established through numerical simulation to predict the assembly process. Furthermore, by employing porous microcarriers loaded with BMSCs and growth factors, and incorporating zonal addition of hydroxyapatite, the proposed Faraday wave multilayer assembly methods were utilized to construct a biomimetic triphasic osteochondral structure (cartilage zone-calcified zone-subchondral bone zone). The constructed structures will be subsequently evaluated comprehensively across multiple dimensions, including cell viability, cell phenotype, matrix expression, protein secretion, mechanical properties, and efficacy in repairing osteochondral defects in a rat model. This study extends the application of Faraday wave bioassembly to the biofabrication of complex three-dimensional tissues, and provides a novel technological pathway for osteochondral regeneration.

Multifunctional Strontium Phosphate Silicate Scaffolds: 3D-Printed Osteogenic Solution for Bone Defects

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Abstract

Objective: Bone defect repair remains a major clinical challenge. Autografts suffer from limited availability and donor-site morbidity, while allografts carry risks of immune rejection, disease transmission and poor morphological adaptation. Consequently, highly biocompatible artificial composite scaffolds have emerged as a research focus. This study developed a novel strontium phosphate silicate ($SrPO_4 \cdot SiO_2$)-modified resin scaffold via digital light processing (DLP)-based 3D printing to provide improved clinical solutions.

Methods: $SrPO_4 \cdot SiO_2$ was surface-modified with a silane coupling agent, then uniformly dispersed in a photosensitive resin matrix. Scaffolds were fabricated via DLP 3D printing. Systematic evaluation of mechanical properties, antibacterial performance, biocompatibility, and osteogenic potential was conducted to assess clinical prospects for bone defect repair.

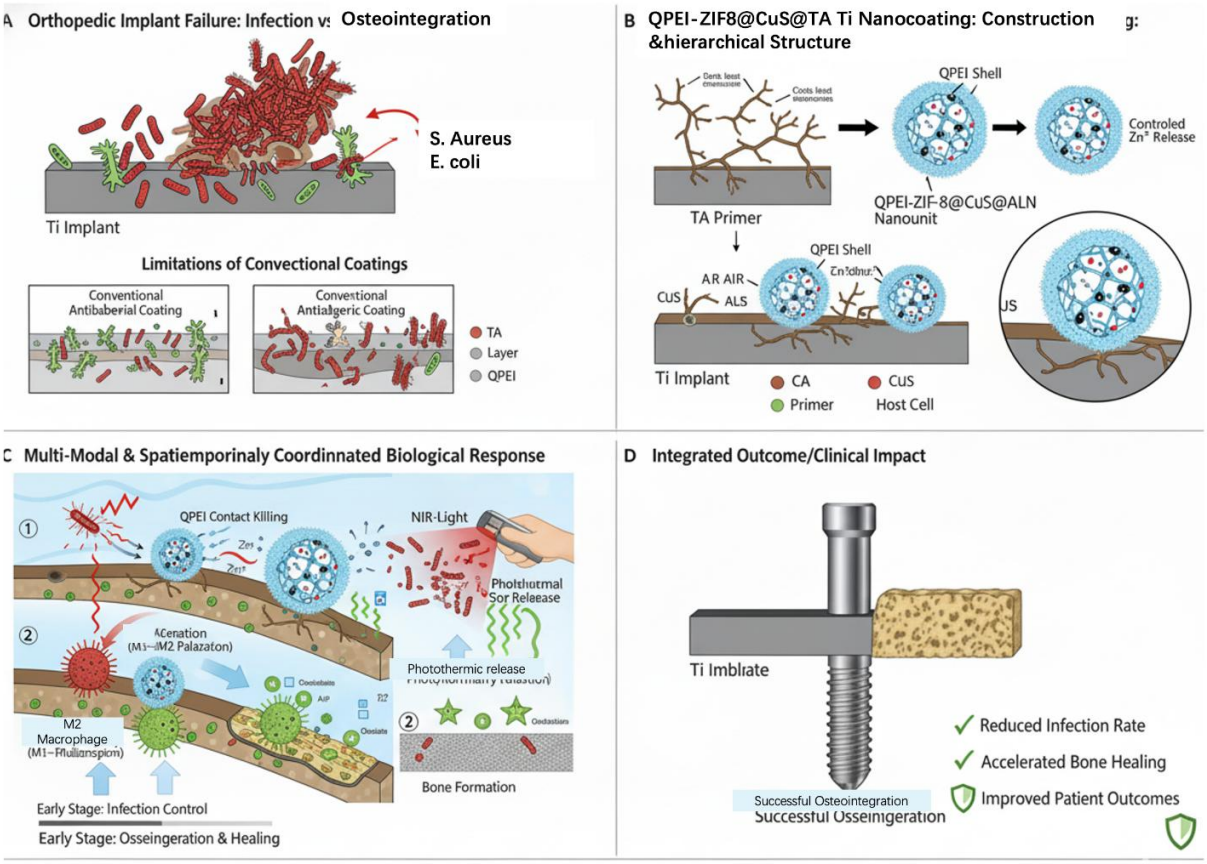
Results: Uniform dispersion of $SrPO_4 \cdot SiO_2$ powder throughout the resin matrix enabled precise fabrication of 3D-printed scaffolds, concurrently enhancing tensile strength and elastic modulus by 144% and 19% versus controls. The scaffold demonstrated antimicrobial efficacy, exhibiting 76% and 56% inhibition against S. *aureus* and E. *coli* respectively, while maintaining exceptional cytocompatibility (CCK-8®). Furthermore, this system significantly stimulated osteogenic differentiation, as evidenced by 52% elevation in alkaline phosphatase (ALP) activity relative to control groups.

Significance: This osteogenic 3D-Printed Strontium Phosphate Silicate-Modified Resin Scaffolds sustains high mechanical strength while demonstrating biocompatibility, antibacterial efficacy, and patient-specific bone regeneration capacity, indicating substantial clinical translation potential.

Keywords: Bone tissue engineering; 3D printing; Strontium phosphate silicate; mechanical properties； scaffold

Dual-Mode Antibacterial ZIF8-Inspired Orthopedic Implant Nanocoating for Biofilm elimination and Osseointegration

Orthopedic implant failure often arises from infection and deficient osseointegration driven by surface-level competition between bacteria and host cells. Conventional coatings provide single-mode antibacterial action, weak spatiotemporal control, limited biofilm removal, and inadequate immune modulation. We present QPEI-ALN/ZIF-8@CuS@TA-Ti, a nanomaterials-centered coating that couples baseline contact killing with on-demand photothermal sterilization and synchronized osteoimmunomodulation. A tannic-acid primer confers robust adhesion and foundational immunoregulation. The programmable core–shell nanounit—ZIF-8 encapsulating CuS and alendronate (ALN), overcoated with quaternized polyethyleneimine (QPEI)—unifies QPEI-mediated contact killing, controlled Zn2+ release, and NIR-triggered CuS hyperthermia for biofilm clearance, while ALN promotes osteogenesis and mitigates cationic cytotoxicity. This dual-mode antibacterial design sustains baseline inhibition for >4 weeks and achieves NIR-boosted antibiofilm activity (>90% disruption). The controlled cascade enhances macrophage M2 polarization and subsequently accelerates osteogenic differentiation. Our coating nanomaterials dynamically interfaces with the preimplant microenvironment to coordinate phased infection control and bone regeneration. These findings position this MOF-inspired nanocoating as a promising, translatable strategy for complex orthopedic indications, with potential to reduce revision rates and healthcare burden in implant-associated infections.



STRUCTURAL REGULATION AND MEDICAL APPLICATIONS OF COLLAGEN

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Tissue regeneration and repair represent pressing challenges in modern healthcare, urgently requiring breakthroughs in regenerative medicine driven by innovations in materials science. As a naturally occurring structural protein in the human body, collagen exhibits excellent biocompatibility, bioactivity, and low immunogenicity, making it a highly promising candidate material in the field of regenerative medicine. However, most currently available clinical collagen-based products suffer from limited functionality. The core issue lies in the significant structural discrepancy between artificially prepared collagen materials and native tissues in terms of complexity. To address this scientific challenge, we have innovatively proposed the use of physical fields to regulate the collagen molecular assembly process, enabling precise control over the microstructural features of collagen, including fiber dimensions, alignment, and spatial distribution. This technology overcomes the limitations of traditional processing methods and successfully constructs collagen material systems with tissue-mimetic structural characteristics, achieving functional regeneration of complex tissues such as alveolar bone, cornea, and tendon. Moreover, we have overcome key technical bottlenecks in the scalable preparation of collagen materials under physical field modulation, thereby facilitating clinical translation and establishing a systematic body of innovative outcomes.

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BIO-NANO RECOGNITION MECHANISM OF NANOSTRUCTURES WITH CELLULAR MEMBRANE

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The bionanoscale recognition event at the cell surface is the first step for cellular programming mechanisms to manage nanoscale objects. Understanding the bionanoscale recognition mediated by the membrane receptor and the dynamic endocytosis process allows us to regulate the downstream biological processes and promote advanced therapeutics, such as escaping liver clearance. However, it has remained challenging to measure the recognition kinetics and capture the dynamic internalization behaviors of nanostructures while also probing the mechanical aspects of the internalization. To address the above key technical challenges, we developed a receptor fusion protein expression system, an atomic force microscopy-based force tracing technique, and homemade AIE-visualized nanoliposomes. We mapped the protein corona-mediated recognition kinetics and mechanism between nanostructures and scavenger receptors, revealed the transmembrane behavior and molecular mechanism of AIE-visualized nanoliposomes regulated by protein corona, explored the transmembrane kinetic process and mechanical properties of gold nanorods with different shapes at the single-particle level, and for the first time, proposed the transmembrane mechanism of rod-shaped nanostructures with "intermittent rotation". This knowledge furthers our understanding of bio-nano interactions and is important for the efficient use of nanomedicines.

Live-Cell Tracking of Specific RNA G-Quadruplex for Stress Sensing by L-RNA Fluorogenic Bifunctional Aptamer

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Abstract

RNA G-quadruplex structures (rG4s) are functionally linked to various physiological processes and thus, monitoring of rG4s dynamic represents a new direction for disease diagnosis and discovery of potent therapeutic targets. Yet, visualizing specific rG4s in live cells remains highly challenging owing to the lack of probes' specificity. Very recently, conventional staining or pull-down methods revealed that cell stresses such as starvation and oxidative stress can significantly alter the folding state of APP rG4s. In this work, we devise a L-RNA fluorogenic bifunctional aptamer, namely, L-Apt.1-1_Pepper, that can specifically light up APP rG4 structure in live cells for stress sensing. Using deconvolution fluorescence microscopy, we showcase in real time that L-Apt.1-1_Pepper specifically allows for stable and bright tracking of endogenous (and transfected) *APP* rG4 but not other structurally similar rG4 motifs in various cancer cell lines. Furthermore, we demonstrate that L-Apt.1-1_Pepper not only fluorescently responds to treatment of distinct G4 ligands, but also to G4-unwinding protein DHX36 on *APP* rG4 folding in live cells. At single-cell level, L-Apt.1-1_Pepper enables the in situ imaging of *APP* rG4 dynamic under starvation and oxidative stress. Our study expands the experimental toolbox for non-invasive visualization of specific rG4, paving a novel way in detecting intracellular status such as stress level.

Selectivity and Stability Reshaping High-Sensitivity Detection Boundaries -Semiconductor SERS Nanobiosensor

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Circulating tumor cells (CTCs), which detach from primary or metastatic tumors and enter the bloodstream, play a critical role in cancer metastasis and are closely associated with patient prognosis. Their detection holds significant clinical potential for early diagnosis, treatment monitoring, drug resistance assessment, and personalized therapeutic strategies. Surface-enhanced Raman scattering (SERS) offers distinct advantages for bioanalysis, including high sensitivity, rapid response, minimal invasiveness, label-free capability, and molecular fingerprinting. In recent years, SERS-based bioprobes have been increasingly applied for the detection of biological targets. In this work, we developed a series of semiconductor SERS bioprobes capable of detecting individual CTCs with an accuracy exceeding 90% in peripheral blood. Here, we present an overview of recent advances in SERS biosensing substrates and highlights high-sensitivity SERS platforms for CTC detection. Special emphasis is placed on the design and application of semiconductor SERS nanomaterials, providing a perspective on future high-performance sensing strategies.

Keywords: SERS, bioprobes, tumor detection, CTCs

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T_H1 CELL-MEDIATED IMMUNE REPROGRAMMING FOR VESSEL NORMALIZATION

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Abstract

Enhanced leakiness of vasculatures has been regarded as a hallmark of tumour progression. However, recent evidence reveals that vascular structure and function are regulated by immune homeostasis. Here, we developed a single-vessel quantitative analysis approach leveraging nanoparticle imaging and a U-Net++–based segmentation framework (Nano-U-Net++). Quantitative analysis of over 100,000 vessels revealed that syngeneic tumors growing in immunocompetent host exhibited normalized vessels compared to the xenograft tumors in immunodeficient mice. Vessel normalization increase tight endothelial junctions and pericyte coverage, reduce vascular permeability, and mitigate hypoxia. We constructed mouse models with T lymphocyte depletion to reveal depletion of $CD4^+$ T lymphocytes decreased vessel normalization. Bioinformatic analyses revealed that gene expression features related to vessel normalization correlate with immunostimulatory pathways, and Type 1 T helper (T_H1) cells play a crucial role in vessel normalization. T_H1 cells secrete interferon-γ to activate the JAK1–STAT1 pathway, which promotes vascular normalization. Normalized vessel would decrease blood flow to mitigate tumor metastasis. Vessel normalization, in turn, facilitates IFN-γ CAR-T cells infiltration, forming a positive feedback loop between vasculature and antitumor immunotherapy. An improved understanding between immune competence and vessel normalization must assess the systemic immune landscape beyond the tumour microenvironment. T_H1 adoptive transfer promotes vascular normalization in immuno-organoid transplantation, which reveals a general role of immune regulation in maintaining vascular homeostasis.

Reprogramming of iPSCs to NPCEC-like cells by biomimetic scaffolds for zonular fiber reconstruction

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【Abstract】Ectopia lentis (EL), characterised by impaired zonular fibers originating from non-pigmented ciliary epithelial cells (NPCEC), presents formidable surgical complexities and potential risks of visual impairment. Cataract surgery is the only treatment method for EL, but it leads to the loss of accommodative power of the lens post-operatively. Furthermore, the challenge of repairing zonular ligaments in situ remains a significant global issue. Ocular tissue and aqueous humour samples from patients with EL were subjected to RNA sequencing and Olink high-throughput proteomic analysis, revealing the downregulation of pathogenic genes (*FBN1*, *MFAP2*) and upregulation of secretory proteins (IL-12, MMP-1). The high expression of *FBN1* and *MFAP2* in NPCECs suggests their potential as candidates for zonular fiber construction; however, the limited availability of donor sources restricts the feasibility of NPCEC transplantation therapy. The reprogramming and directional differentiation of induced pluripotent stem cells (iPSC) to NPCEC was successfully achieved using the developed biomimetic scaffolds that mimic the microstructures of natural radial zonular fibers. Excitingly, the single injection of induced NPCEC-like cells significantly contributed to restoring and enhancing mechanical properties in zonular fiber structures in a rabbit model with EL. This proposed in situ iPSC-based regeneration technique might serve as an innovative therapeutic strategy for clinical EL patients, reduce the cataract surgery rate, and retain the adjustment capacity of inherent lentis.

【Keywords】Ectopia lentis, Zonular fiber reconstruction, Induced pluripotent stem cells, Biomimetic scaffolds, In situ regeneration

【Learning objective and Submission details】This novel study used high-throughput techniques to analyze the capsular tissue and aqueous humour of patients with EL, revealing significant differences in the mRNA and protein expression of various genes compared to individuals without lens dislocation. The findings indicated degenerative changes in the extracellular matrix and marked activation of inflammatory pathways in the EL-affected eyes. A biomimetic strategy was implemented to promote the repair of the compromised ocular suspensory ligament. This study is the first to investigate the seeding of iPSCs on a biomimetic radially electrospun scaffold that emulates the lens suspensory ligament. Furthermore, the iPSCs were induced to differentiate into NPCEC-like cells with an NPCEC phenotype using a specialized culture condition. This approach not only addresses the challenge of the limited availability of primary NPCEC but also establishes a targeted method for the directed differentiation of terminal eye cells. This study introduces a stem cell repair strategy that is crucial for the treatment of EL, representing a revolutionary new therapeutic approach for this and potentially other ocular diseases.