NIR-II Light Triggered Burst-Release Cascade Nanoreactor for Precise Cancer Chemotherapy

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Abstract:
The current strategy of co-delivering copper ions and disulfiram (DSF) to generate cytotoxic CuET faces limitations in achieving rapid and substantial CuET production specifically in tumor lesions. To overcome this challenge, we introduce a novel burst-release cascade reactor composed of phase change materials (PCMs) encapsulating ultrasmall $Cu_{2-x}Se$ nanoparticles (NPs) and DSF (DSF/$Cu_{2-x}Se$@PCM). Once triggered by second near-infrared (NIR-II) light irradiation, the reactor swiftly releases $Cu_{2-x}Se$ NPs and DSF, enabling catalytic reactions that lead to the rapid and massive production of $Cu_{2-x}Se$-ET complexes, thereby achieving in situ chemotherapy. The mechanism of burst reaction is due to the unique properties of $Cu_{2-x}Se$ NPs, including their small size, multiple defects, and high surface activity. These characteristics allow DSF to be directly reduced and chelated on the surface defect sites of $Cu_{2-x}Se$, forming $Cu_{2-x}Se$-ET complexes without the need for copper ion release. Additionally, $Cu_{2-x}Se$-ET has demonstrated a similar (to CuET) anti-tumor activity through increased autophagy, but with even greater potency due to its unique two-dimensional-like structure. The light-triggered cascade of interlocking reactions, coupled with in situ explosive generation of tumor-suppressive substances, mediated by size and valence of $Cu_{2-x}Se$, presents a promising approach for the development of innovative nanoplatforms in the field of precise tumor chemotherapy.

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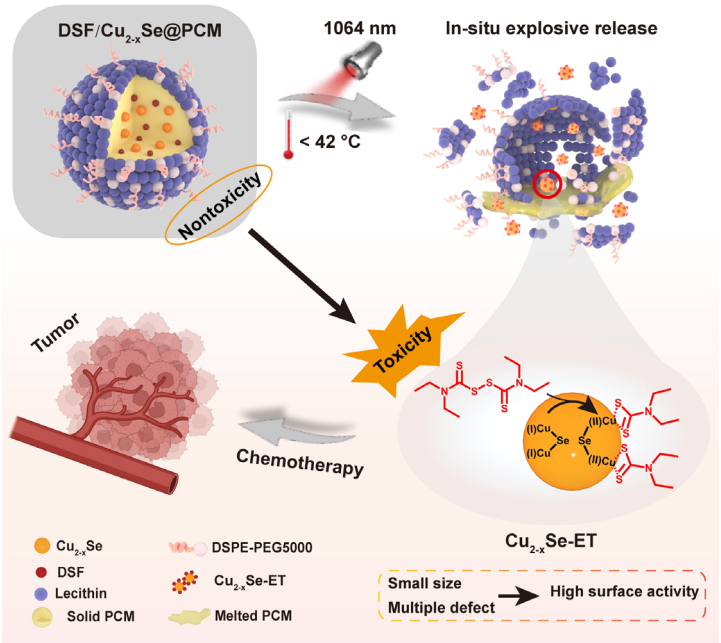

Study on construction and characterization of zinc-doped nano-hydroxyapatite/gelatin scaffold

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Abstract:

Objective: Our previous studies have shown that appropriate concentration of zinc ions could regulate the immune balance of Th17/Treg lymphocytes in vitro, promote osteoblast differentiation and bone minerals deposition. This study was intented to construct and characterize a zinc-doped nano-hydroxyapatite/gelatin(Zn-nHA/Gel) composite scaffold.

Methods: Zinc-doped nano-hydroxyapatite (Zn-nHA) was prepared by wet chemical precipitation method, and Zn-nHA/Gel was obtained by crosslinking gelatin with EDC/NHS. The surface and cross section morphology were observed by SEM, and the elemental composition was detected by EDS. The crystal structure was analyzed by XRD, and the functional groups was analyzed by FTIR. The thermal stability and organic/inorganic ratio were analyzed by TG, DTG and DSC. The physicochemical properties were analyzed by water absorption, pH detection and degradation. The in vitro biocompatibility of CCK-8 was evaluated, and the controlled release efficiency of zinc ion was investigated.

Results: The results of SEM, EDS and XRD showed that the composite scaffold was multi-layered porous structure and zinc ion was successfully loaded onto the composite scaffold material. FTIR results indicated the formation of chemical bonds between organic and inorganic components. TG, DTG and DSC demonstrated good thermal stability. Water absorption rate, pH detection, degradation rate, CCK-8 results indicated good physicochemical properties and biocompatibility of the Zn-nHA/Gel composite scaffold. The result of zinc controlled release test showed a cumulative released zinc ion concentration of 132.62 μM, which was consistent with the optimal concentration *in vitro*.

Conclusion: The prepared Zn-nHA/Gel composite scaffold material has good physicochemical properties and *in vitro* biological compatibility, as well as favorable controlled release of zinc ion.

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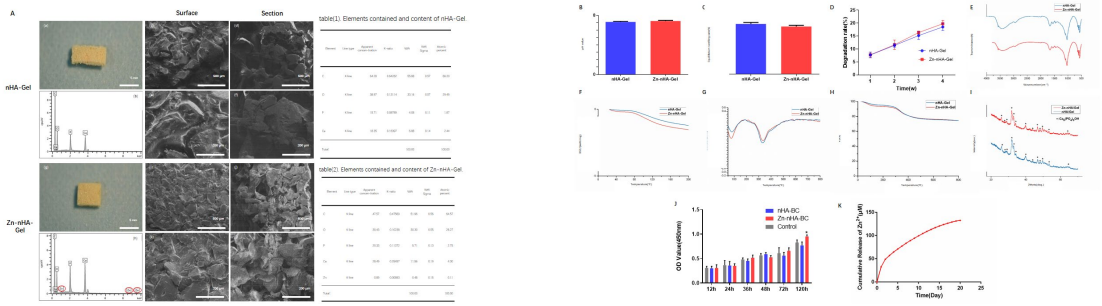

Physical and chemical characterizations of Zn-nHA/Gel with SEM/EDS(A), pH, swelling rate, degradation rate, FTIR, TG, DTG, DSC(B-I), CCK-8(J) and release efficiency of zinc ion(K)

A Hydrogel-Based System for Mimicking Oxygen Gradients in Periodontal Pockets

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Abstract

Background: Periodontitis is a chronic inflammatory disease that poses significant risks to both dental and systemic health. Traditional *in vitro* models fall short in replicating the complexity of the oral microbiome within periodontal pockets. This study develops a scalable hydrogel-based platform using jammed-packed microgel (JPM) to locally regulate oxygen tension. **Methods:** JPM was acquired through dispensing carbomer in a liquid medium to form a semi-solid, gel-like matrix. We characterized its rheological properties, mass transport capabilities, and oxygen control to assess the feasibility of constructing this model. The hydrogel's biocompatibility was evaluated using OD600 measurements, crystal violet staining, live/dead assays, and scanning electron microscope (SEM) with oral bacteria cultured within the hydrogel. Immunostaining was also used to examine biofilm formation in JPM under varying oxygen levels, confirming the hydrogel's ability to locally regulate oxygen in culture. **Results:** The physical properties of JPM suggest it is well-suited for creating a semi-solid *in vitro* model that allows for material exchange and oxygen regulation within the hydrogel. Biocompatibility tests confirmed that JPM does not significantly inhibit oral microbial growth and may positively enhance biofilm formation. Co-culture experiments under varying oxygen conditions within the hydrogel further validated the platform's potential for localised oxygen control. **Conclusions:** This study demonstrates the feasibility of using hydrogels to control localised oxygen environments and support oral microbial cultures, effectively recreating the complex oxygen conditions and gradients present in periodontal pockets. This hydrogel platform offers a cost-effective, scalable solution for studying periodontitis and developing new treatments, with potential applications in broader contexts, including the development of pathological models and advancements in clinical diagnostics.

Bioinspired Nanotexturing of Dental Implants Towards Bioactivity and Bactericidal Functions

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Abstract:
Advanced techniques like lithography, hydrothermal processes, and laser patterning have been employed to create bioinspired nanotextured titanium implants, which can modulate cellular functions to enhance bioactivity and antibacterial properties. However, these methods are often expensive and involve multiple steps, limiting their practical application in clinical settings and on benchtop implant modifications. For the first time, this study introduces a single-step, cost-effective, and clinically translatable approach—electrochemical anodization—to create bioinspired nanopillar-like textures on micro-rough titanium surfaces. Detailed surface characterization reveals the formation of unique nanostructures, including nanoscale Spinules, Daggers, Papillae, Spikes, and Flames, each with distinct roughness and wettability properties. Subsequent experiments involve culturing primary human osteoblasts and polymicrobial salivary biofilm on the nanotextured implant surfaces. The results show that these nanotextures significantly enhance protein adhesion while supporting osteoblasts' proliferation, adhesion, and spreading. Additionally, all nanotextured surfaces demonstrate superior antibiofilm properties compared to control surfaces. In summary, this single-step anodization technique offers a promising, cost-effective, and scalable approach to creating bioactive and antibacterial nanotextures on implant surfaces, with strong potential for clinical translation in the next generation of dental implants.

Biomimetic Surface Nanoengineering of Zinc Implants for Improved Biocompatibility and Immune Modulation

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Abstract: Zinc (Zn) is emerging as a promising biodegradable material for dental and craniofacial implantology due to its tunable biodegradability and essential roles in cellular activity and tissue repair. However, its clinical application is limited by poor biocompatibility. Our study addresses this challenge using a novel biomimetic strategy that employs surface nanoengineering to create nano-geometric structures and chemical compositions through controlled exposure to Dulbecco's Modified Eagle Medium (DMEM). This approach enables the customization of Zn implant degradation rates. The nanostructured surfaces enhance primary human osteoblast attachment, proliferation, and differentiation, and improve macrophage functionality by fostering a shift from a pro-inflammatory M1 to a reparative M2 phenotype. In vivo experiments demonstrate that these surface-engineered implants significantly promote tissue integration through M2 macrophage polarization, resulting in a favorable immunomodulatory environment and increased collagen formation. Proteomic analysis indicates that the tissues around the engineered Zn implants are enriched with involved in key biological mechanisms of wound healing, such as cell adhesion, cytoskeletal structural arrangement, and immune response. This study underscores the potential of surface-engineered Zn implants to improve biocompatibility and anti-inflammatory properties, with significant implications for the clinical translation of biodegradable Zn-based implants in craniofacial and dental applications.

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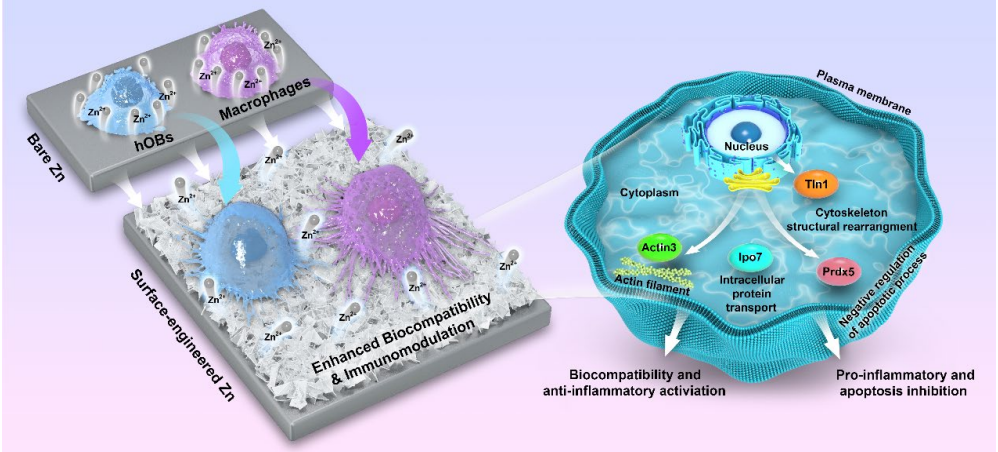

Enhanced penetration efficacy of ferromagnetic nanoparticles loading minocycline against periodontal biofilms

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Objectives: The key factor for the periodontitis therapy is to thoroughly eliminate the dental plaque biofilm especially including the deep periodontal tissue. Antibiotics can penetrate deep periodontal tissue, but bacterial biofilms are difficult to penetrate because of their polysaccharide matrix, often requiring doses up to 1,000 times higher than those of suspended bacteria. In order to effectively penetrate the biofilm, we constructed a Fe3O4 magnetic nanoparticle loading minocycline (FPM NPs) to physically penetrate the biofilm under the magnetic force for effectively eliminating dental plaque biofilm.
Methods: The ferromagnetic nanoparticles were prepared by reducing Fe3+ under the protection of nitrogen, and then loaded with minocycline. The particle size and dispersion of the nanoparticles were characterized by transmission electron microscope, scanning electron microscope and dynamic light scattering, and the drug loading efficiency was determined. In order to verify the magnetic targeting of FPM NPs, the antibacterial effects under magnetic field and non-magnetic field were tested. Furthermore, the therapeutic effect of FPM NPs on periodontitis in rats was also investigated.
Results: The results indicated that FPM NPs exhibited good chemical stability and biocompatibility. The multifunctional nanoparticles exerted strong anti-biofilm activity against Streptococcus Sanguis, Porphyromonas Gingivalis and Fusobacterium Nucleatus under magnetic field. The inflammation recovered well in rats after treatment. It also has real-time monitoring function and magnetic targeting capability.
Conclusions: The ferromagnetic nanoparticles provide a new idea for the treatment of clinical periodontitis and provides theoretical basis and experimental support for the clinical application of magnetic targeted nanoparticle.

VDAC1 regulates osteoblast differentiation and autophagy in periodontitis

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Abstract

Objective: Periodontitis has been demonstrated to induce dysregulation of autophagy in osteoblasts, accompanied by mitochondrial dysfunction. The objective of this study was to investigate the potential role of the mitochondrial protein VDAC1 in regulating osteoblast differentiation and autophagy in periodontitis.

Methods: MC3T3-E1 cells were cultured and four experimental groups were established: control group, LPS group, VDAC1 overexpression group, and VDAC1 overexpression + LPS group. The ALP activity assay, ALP staining assay, alizarin red staining assay, and Western blot assay were employed to detect osteogenic marker proteins, thereby determining the degree of osteogenic differentiation. The lysosomal staining assay and Western blot assay were used to detect P62 and LC3, with the objective of determining the level of autophagy and investigating whether VDAC1 exerts a regulatory effect on osteogenic differentiation and its effect on the regulation of autophagy.

Results: The VDAC1 overexpression group exhibited elevated expression of the osteogenic marker proteins ALP, RUNX2, and OCN, enhanced ALP activity, and more intense ALP and alizarin red staining, in comparison to the control group. Compared with the control group, treatment with 10 μg/ml LPS resulted in a reduction in the ratio of LC3 II/I, an increase in P62, and a decrease in the number of lysosomes in MC3T3-E1 cells. Conversely, the VDAC1 overexpression group demonstrated an increase in LC3 II/I, a reduction in P62, and an increase in the number of lysosomes in comparison to the control group.

Conclusion: The inhibitory effects of periodontitis on osteoblast differentiation and autophagy are antagonized by VDAC1.

Detecting and reconciling mitochondrial metabolism for diagnosis and treatment of osteoarthritis via curcumin-derived carbon dots

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Abstract:
Osteoarthritis(OA) is a degenerative disease with complex etiologies that imposes a huge physical and economic burden on patients. However, developing effective means of preventing or delaying OA remains an unmet goal. Mitochondrial dysfunction is a common and important incentive in OA. In this work, the anti-inflammatory and antioxidant drug curcumin was utilized as a precursor to prepare ultra-small-sized (~2 nm) carbon dots(Cur-CDs). Cur-CDs had good water-solubility and fluorescence properties, not only improving the difficult problem of inefficient administration of the hydrophobic drug curcumin but also fluorescently imaging cellular mitochondria. *In vitro* experiments have shown that Cur-CDs could successfully target to the mitochondria of chondrocytes and bone marrow macrophages, and alleviate mitochondrial dysfunction by reducing reactive oxygen species levels. *In vivo* experiments showed that the group treated by Cur-CDs significantly attenuated articular cartilage damage, reduced osteoclastogenesis, promoted collagen regeneration, and inhibited osteoclast differentiation, thereby alleviating the process of osteoarthritis. In summary, Cur-CDs regulated cartilage-bone metabolism by detecting and alleviating cellular mitochondrial dysfunction for the prevention and treatment of osteoarthritis.

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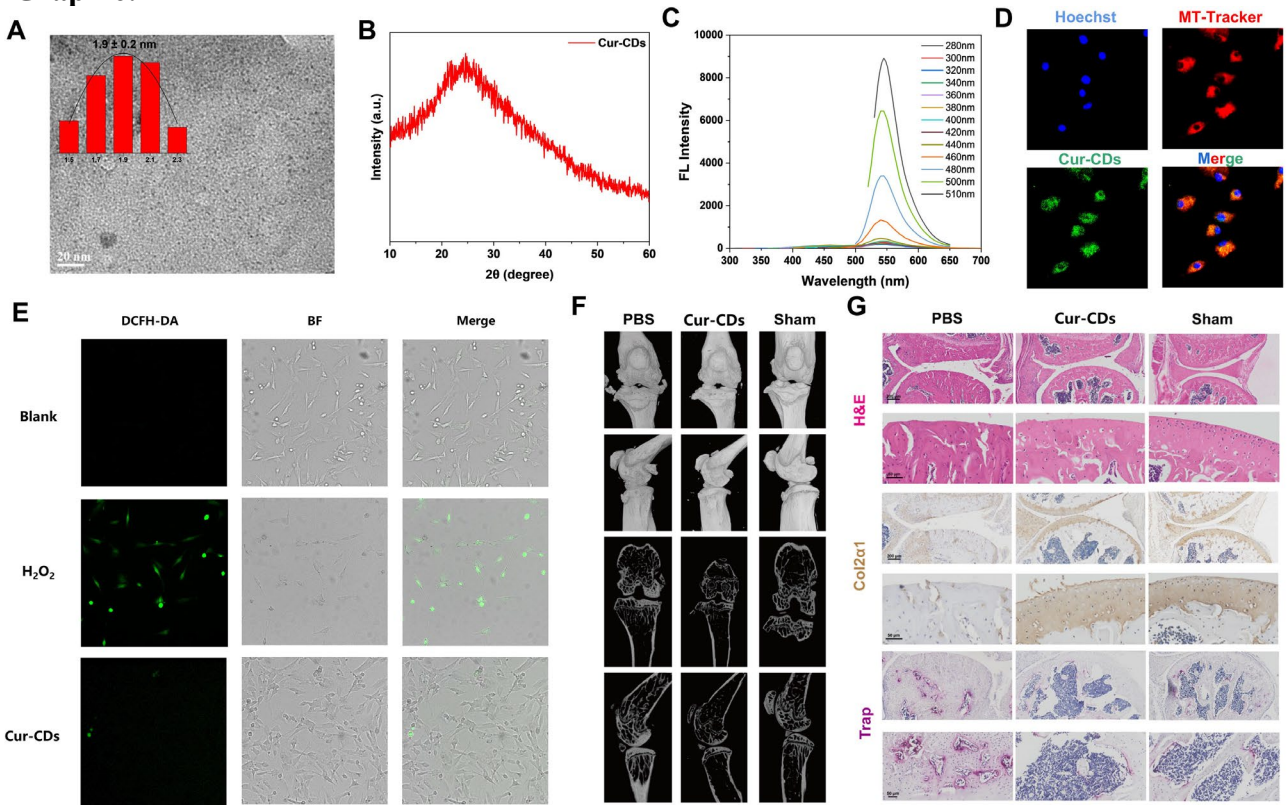

A Comparative Study of Osseointegration of Two Different Thread Designs of Dental Implants in the Canine Jaw

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Abstract:

Objective: To evaluate the osseointegration of dental implants with different thread designs in the canine mandible.

Methods: Four male beagle dogs were selected for the study. Bilateral mandibular premolars and molars (PM2-M2) were extracted and allowed to heal for 12 weeks. The test group consisted of newly designed dental implants, while the control group used AstraTech OsseoSpeed™ TX implants (Fig.a). Four implants were placed on each side of the mandible using a split-mouth design, with submerged healing. Two animals were sacrificed at 2 weeks and the remaining two at 12 weeks post-surgery (n=8). Radiological and histological evaluations were conducted using intraoral digital X-rays and non-decalcified hard tissue sections.

Results: Radiological imaging showed similar bone healing in both groups at 2 and 12 weeks post-surgery (Fig.b). Histologically, at 2 weeks, the implants were primarily mechanically stabilized within the host bone, with limited new bone formation around the implants (Fig.c). By 12 weeks, extensive trabecular-like, fully mineralized bone had formed around the implants. The bone-implant contact (BIC%) was (46.69 ± 8.47) % in the test group and (36.71 ± 13.72) % in the control group at 2 weeks, and (67.27 ± 7.46)% and (56.63 ± 8.31)% at 12 weeks, respectively, with no statistically significant difference between groups(Fig.d).

Conclusions: Both dental implants with different thread designs achieved satisfactory and comparable osseointegration in the canine mandible.

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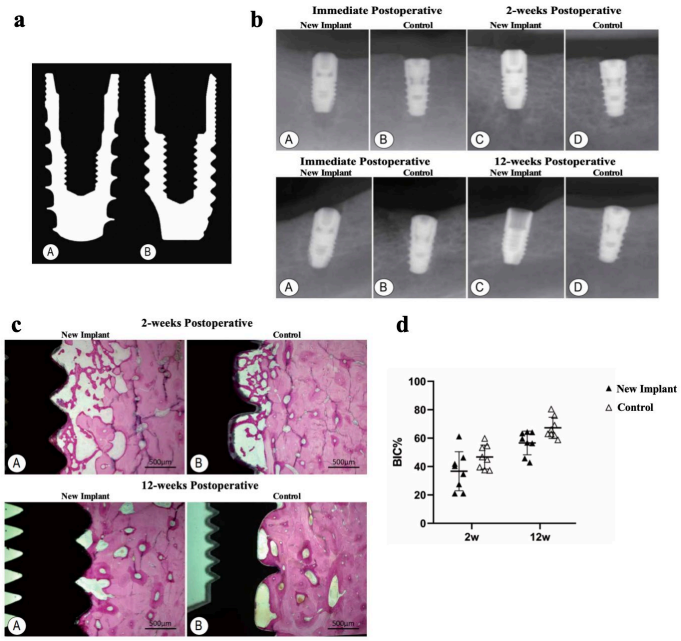

(a)Dental implants with two different thread designs. A: Test group; B: Control group. (b) Radiographic examination of implants in both groups. (c) Histological sections of implants in both groups. (d) Bone-to-implant contact (BIC) rates of the two implant types

Effects of obesity on alveolar bone resorption and gut microbiota in periodontitis mice

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Abstract: Objective To study the effects of obesity on alveolar bone loss and gut microbiota in mice with periodontitis. **Methods** Twenty-four eight-week-old female C57BL6/J mice were randomly divided into four groups based on table of random numbers (n=6 in each group): normal diet group (NFD), in which mice were given normal chow diet; high-fat diet group (HFD), in which mice were given high-fat diet; normal diet +periodontitis group (NFD_PD), in which mice were fed with normal food diet and induced to periodontitis by ligating the bilateral maxillary second molars with 5-0 silk thread at the fourth week; high-fat diet +periodontitis group (HFD_PD), in which mice were fed with high-fat diet and periodontitis was induced at the fourth week. The mice of four groups were recorded body weight weekly. The mice were euthanized for collecting the samples at the end of the 12th week. Liver, kidney, perirenal and retroperitoneal fat were collected and weighed. Serum was collected to detect the changes of blood lipids, inflammatory factor and bone metabolism markers. The right maxilla bones were scanned by micro-computed tomography (micro-CT.) HE staining and TRAP staining were detected to observe the periodontal tissue. The cecum contents were collected for gut microbiota 16S rRNA gene sequencing. Pearson correlation analysis was performed to analyze the correlation between the abundance of gut microbiota and serum inflammatory and bone metabolism markers. **Results** After 12 weeks of high-fat diet fed, the body weight, perirenal and retroperitoneal fat, kidney and liver weight of HFD group were significantly higher than those of NFD group (P<0.01); Serum levels of TC, TG and LDL in HFD group were significantly higher than those in NFD group (P<0.01). Compared with NFD_PD group the linear distance from the alveolar bone crest to the enamel cementum junction on the mesial site of maxillary second molar in HFD_PD group was significantly increased (P<0.001). HE staining showed that the maxillary second molar attachment loss, collagen fiber destruction and inflammatory cell infiltration were more significant serious in HFD_PD group compared with NFD_PD group. The number of TRAP staining positive cells in HFD_PD group was higher than that in NFD_PD group (P<0.05). The levels of IL-1β, IL-6 and MCP of serum in HFD_PD group were significantly higher than those in NFD_PD group (P<0.01); The RANKL/OPG value of serumin HFD_PD group was higher than that in NFD_PD group (P<0.01)]. The 16S rRNA gene analysis revealed that the *Bacteroides*/*Firmicutes* ratio in HFD_PD group was significantly higher than that in NFD_PD group (P=0.03)]. The abundance of *Oscillospira* in HFD_PD groupwas significantly higher than that in NFD_PD group (P<0.001)]. The β-diversity analysis of gut microbiota based on Bray-Curtis distance showed that samples of HFD_PD group and NFD_PD group were obviously grouped. Correlation analysis showed that the abundance of *Oscillospira* was significantly positively correlated with IL-1β, IL-6, MCP concentration and RANKL/OPG value in serum (r values were 0.79, 0.81, 0.69, 0.64, P<0.05).**Conclusions** Obesity promotes alveolar bone resorption in periodontitis mice and changes the gut microbiota. *Oscillospira* may play a key role.

Bendable Vessel-on-a-Chip Models for Coronary Artery Disease

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Abstract:

Introduction: Coronary arteries experience cyclic bending due to the rhythmic motion and compression of the heart during each cardiac cycle and the cyclic bending contributes to significant changes in blood flow and mechanical stress in coronary plaque, which may impact plaque progression and rupture risk[1]. Current studies on the effects of cyclic bending are only computational simulations and this is a lack of in vitro experiments to replicate the physiological conditions and the cyclic motion of coronary arteries.

Aim: This study aims to evaluate the impact of stenotic coronary artery's cyclic bending on plaque formation and progression.

Method: To mimic the cyclic bending of a coronary artery, a soft fluidic actuator with fast Pneumatic Nets was designed and fabricated. A static stenotic coronary artery microfluidic model was scaled down to microfluidic size for cell attachment and perfusion while matching physiological wall shear stress. The chip was 3D printed using Lumen X bioprinter (Cellink, USA) with gelatin methacryloyl (GelMA) photoink. By integrating the soft robotic actuator and vessel chip, the system can be used to investigate endothelial dysfunction by cell number, orientation, monocyte adhesion and low-density lipoproteins uptake.

Result: The deformation or bending angle of the soft actuator was found to be dependent on number of PneuNet, thickness of strain limiting layer, wall thickness and material properties. The coronary artery model was scaled down by 2.5 folds by dimensional analysis and computational fluid dynamics which was validated with micro-Particle Image Velocimetry (μPIV). The hydrogel can be accurately printed with 100μm and 50μm layer height.

Conclusion: Our study so far lays a foundation to further investigate the impact of stenotic coronary artery and its cyclic bending on plaque formation and progression.

Figure 1

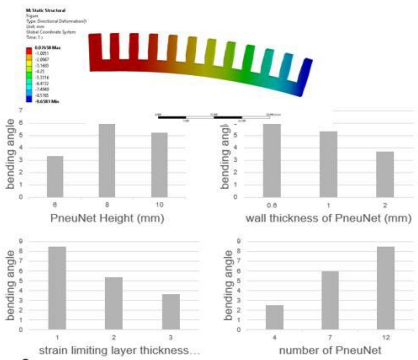


Figure 2

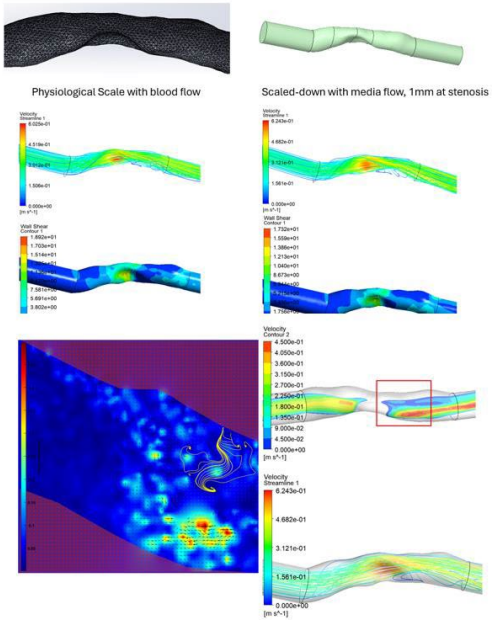
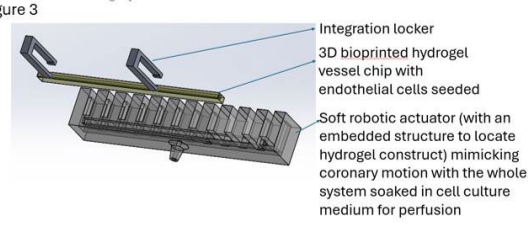


Figure 3



Enhanced π-conjugation in hybridized local and charge transfer state by intramolecular hydrogen bonding to construct efficient red emitters for OLEDs and cellular imaging

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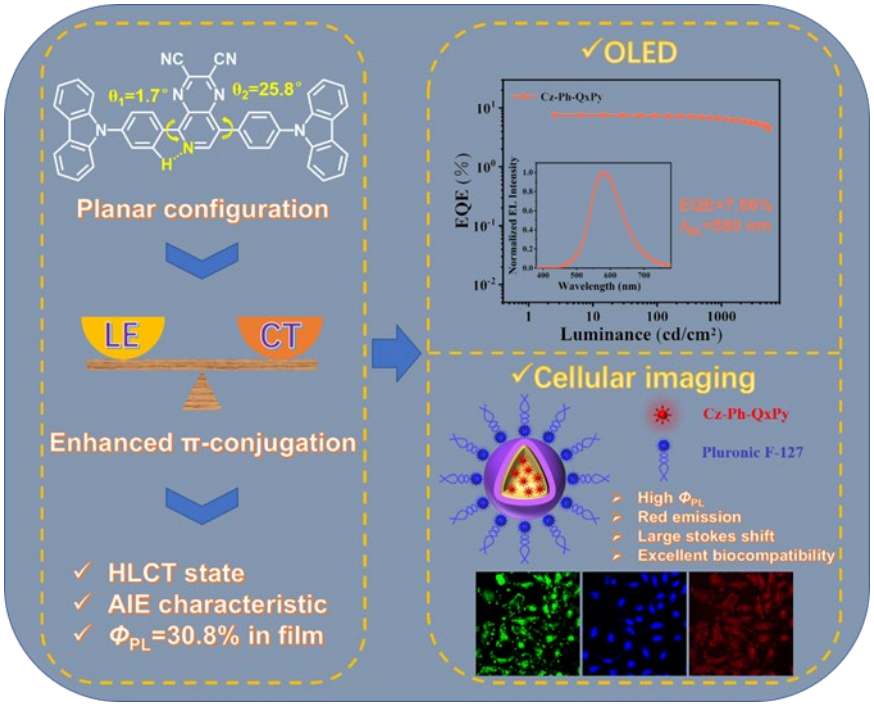
Abstract:

Red emitting materials are the key to development of organic light-emitting diodes (OLEDs) and bioimaging, but limited by the energy gap law and aggregation-caused quenching (ACQ), impeding their applications. Herein, two red emitters **TPA-QxPy** and **Cz-Ph-QxPy** were designed and synthesized with aggregation-induced emission (AIE) characteristics. **TPA-QxPy** had a strong charge transfer (CT) state, while due to the different spatial configurations of the donor units, intramolecular hydrogen bonds were formed in the **Cz-Ph-QxPy**, enabling the locally excited (LE) state to be incorporated into CT emissive state to form hybridized local and charge-transfer (HLCT) state. The results demonstrated that the higher planarity of the **Cz-Ph-QxPy** enhanced the π-conjugation and hybridization between the CT and LE, showing a red emission at 600 nm and a high fluorescence quantum yield of (Φ_{PL}) 30.8% in film. **Cz-Ph-QxPy**-based OLED achieved highly efficient red emission with external quantum efficiency (EQE) of 7.56% at 580 nm. Moreover, benefiting from AIE characteristics, the fabricated **TQx NPs** and **CQx NPs** with near-infrared (NIR)/red emission showed high photostability and biocompatibility and were successfully used for cellular imaging. This work provides new insights for promoting the luminescence performance of red emitting materials with HLCT state by spatial configuration changes.

Graphic:



Biodegradable porous Zn-1Mg-3βTCP scaffold for bone defect repair: *In vitro* and *in vivo* evaluation

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Abstract:

Zn-based materials are promising as bone repair materials, but their poor mechanical property and bioactivity as well as low degradation rate render the potential application. Rational structural and material design can address the concerns. In this study, porous Zn-1 wt.%Mg-3 vol.%β-TCP scaffolds with 40% and 60% preset porosities were fabricated via heating-press sintering using NaCl particles as space holders, and their mechanical properties, *in vitro* degradation behavior, cytotoxicity and *in vivo* osteogenic activities were evaluated. The results showed that the actual porosities of the scaffolds were 22% and 50%. Mg exists in the form of Zn_2Mg and $Zn_{11}Mg_2$, while β-TCP evenly distributed in the matrix. The compressive yield strength of scaffolds ranges from approximately 58.46 to 71.04 MPa, which is close to that of cancellous bone. The *in vitro* degradation tests showed that the corrosion rate of the scaffolds was in the range of about 2.73-4.28 mm/y. Moreover, the scaffolds not only provided great space for osteoblasts adhesion and proliferation *in vitro*, but also possessed favorable degradability and osteogenic activity *in vivo*. The porous Zn-1 wt.%Mg-3 vol.%β-TCP scaffolds manifest reliable mechanical properties, desirable degradability and osteogenic activity, which are promising as next-generation bone repair materials.

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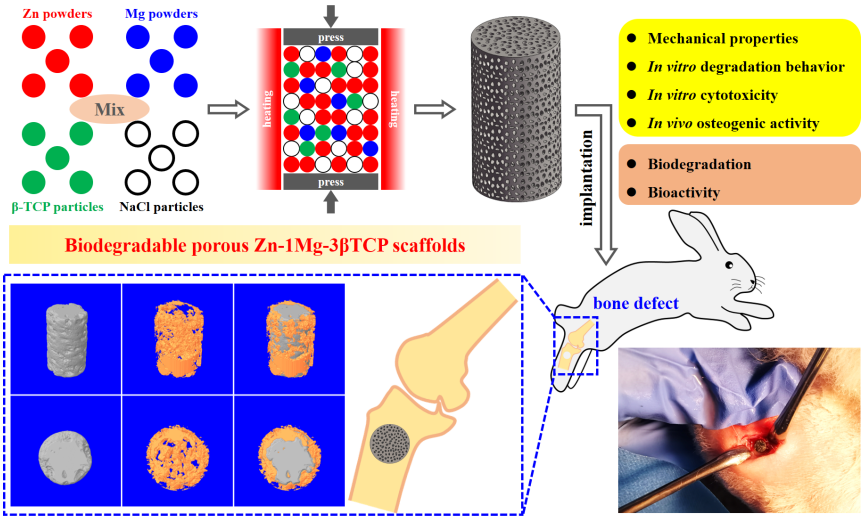

The composite of fluorinated porcine hydroxyapatite/collagen biomaterials including osteogenic performance evaluation *in vitro* and *in vivo*

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Abstract:

Objective:

This study evaluates the osteogenic potential of fluorinated porcine hydroxyapatite (FPHA) combined with collagen at different concentrations (10%, 20%, 30%). It aims to assess cell growth, scaffold stability, and bone regeneration both *in vitro* and *in vivo* to identify the optimal collagen concentration for tissue engineering.

Methods:

FPHA/Collagen scaffolds with varying collagen concentrations (10%, 20%, 30%) were evaluated *in vitro* and *in vivo*. *In vitro*, MC3T3-E1 cells were cultured on the scaffolds, and cell viability was measured using the CCK-8 assay on days 1, 3, 5, and 7. SEM imaging at 1000× and 2000× magnifications analyzed scaffold microstructure and cell attachment. *In vivo*, the scaffolds were implanted in SD rat calvarial defects, with bone regeneration assessed over 4 weeks through histological analysis.

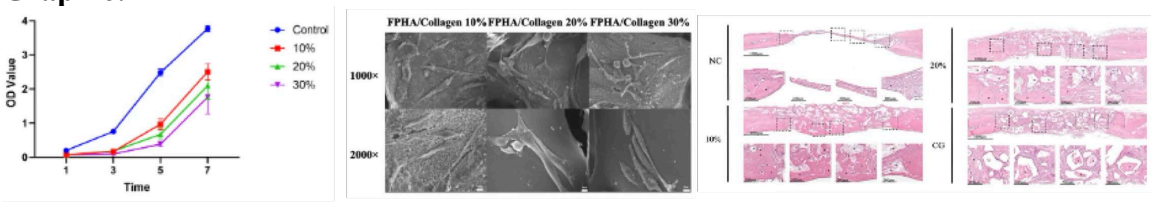
Results:

The 10% collagen scaffold showed better cell proliferation in the CCK-8 assay, with higher OD values at days 5 and 7 compared to the 20% and 30% scaffolds. SEM images showed more uniform cell distribution, with improved adhesion and growth. *In vivo*, the calvarial defect model also showed enhanced bone regeneration in the 10% group, with prominent new bone formation in histology analyses.

Conclusion:

The FPHA/Collagen 10% scaffold showed the best balance of structure, cell growth, and bone regeneration, supporting optimal cell attachment and bone formation. It holds promise for future tissue engineering applications.

Graphic:



a) **b)** **c)**

CCK-8

a) Over time, the 10% collagen group exhibited superior cell proliferation compared to the other groups, indicating the best biocompatibility.

SEM Images

b) At 1000x and 2000x magnifications, the surface of the 10% collagen composite appeared more uniform and better suited for cell attachment and growth.

Histological Analysis:

c) The 10% collagen group showed better bone tissue regeneration and milder inflammatory responses compared to the others.

2-DG Regulates Immune Imbalance on the Titanium Surface after Debridement

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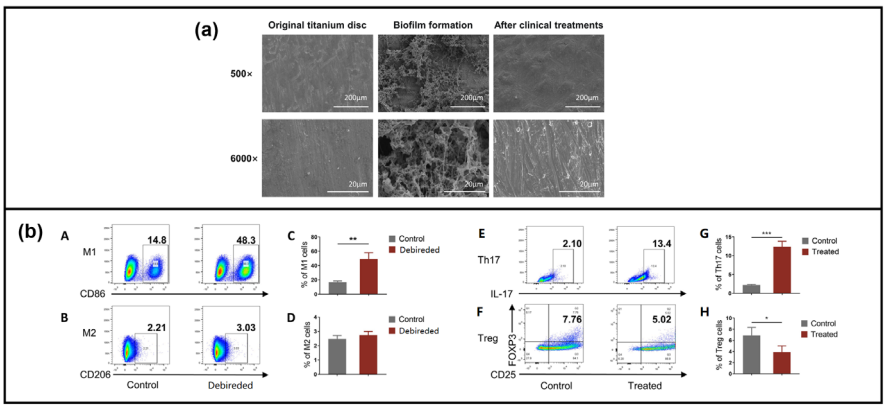
Abstract:
Objectives: Peri-implantitis requires clinical treatments comprised of mechanical and chemical debridement to remove bacterial biofilms. Bone regeneration on the titanium surface after debridement has been a topical issue of peri-implantitis treatments. Increasing evidence has revealed that the immune microenvironment plays a key role in regulating the bone regeneration process. The aim of this study is to explore what kind of immune microenvironment the titanium surface induces after debridement and try to optimize the immune microenvironment.
Methods: In the study, model titanium surface after debridement was prepared via biofilm induction and mechanical and chemical debridement in vitro. Then, the macrophages and naïve CD4+ T lymphocytes were cultured on the titanium surface after debridement for immune microenvironment evaluation, with the original titanium surface as the control. Next, to regulate the immune microenvironment, 2-DG, a glycolysis inhibitor, was further incorporated to regulate macrophages and CD4+ T lymphocytes at the same time.
Results: Surface characterization results showed that the bacterial biofilms were completely removed, while the micro-morphology of titanium surface altered after debridement, and the element composition did not change (Fig.a). Compared with the original titanium disc, titanium surface after debridement can lead to the inflammatory differentiation of macrophages and CD4+ T lymphocytes (Fig.b). The percentage of M1 and Th17 inflammatory cells and the expression of their inflammatory factor genes are upregulated. However, 0.3 mmol of 2-DG can significantly reduce the inflammatory differentiation of both macrophages and CD4+ T lymphocytes and inhibit their expression of inflammatory genes.
Conclusions: Although bacterial biofilms were removed from titanium surface after debridement, the changed surface could still induce immune imbalance and form an inflammatory immune microenvironment. However, this inflammatory immune microenvironment can be effectively reversed by 2-DG in vitro, thus creating an immune microenvironment conducive to osteogenesis, which might provide a new perspective for future therapy of peri-implantitis.

Graphic:



(a) SEM of the titanium surface.
(b) Flow cytometry of macrophages and CD4+ T lymphocytes cultured by original and debrided titanium disc.

Immunomodulatory Cerium-Doped ZIF-62 Nanomaterials: Advancing Periodontal Tissue Regeneration

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Abstract:

Background: Periodontitis, characterised by infection-induced inflammation, results in the destruction of periodontal tissues and is the leading cause of adult tooth loss. The dysregulation of the local immune response reduces the regenerative capacity of the periodontium, highlighting the need for immune modulation to restore periodontal function (1). Advances in immunomodulatory biomaterials have shown promise in repairing and regenerating damaged periodontal tissues. Zeolitic Imidazolate Framework-62 (ZIF-62), known for its large accessible pore area and notable stability, enhances ion-releasing capacity. Studies have shown that Zn2+ released from ZIFs exhibits both antibacterial and pro-osteogenic effects, making ZIF-62 a promising candidate for periodontitis treatment (2). However, nanomaterials can induce reactive oxygen species (ROS), triggering inflammation. Cerium, recognised for its ability to reduce ROS through free radical scavenging and immunomodulation, presents a potential solution (3). We hypothesise that cerium-doped ZIF-62 can regulate immune responses and create a pro-regenerative microenvironment for periodontal tissue regeneration. **Methods**: Ce-ZIF-62 was fabricated through hydrothermal methods and characterised using SEM, TEM, EDX, ICP-MS, and THz/Far-IR. The biocompatibility and immunomodulatory effects of Ce-ZIF-62 on murine macrophages were evaluated using Alamar blue assay, RT-qPCR, and immunofluorescence staining. The antibacterial properties against oral biofilms were investigated using crystal violet and Live-Dead assays. The pro-regenerative properties of Ce-ZIF-62 on periodontal ligament cells were evaluated through alkaline phosphatase activity, Alizarin Red S staining, and RT-qPCR. **Results**: Ce-ZIF-62 was successfully fabricated, displaying a smooth, rounded morphology with uniform dispersion of zinc and cerium ions. Beyond supporting normal cell growth, Ce-ZIF-62 reduced pro-inflammatory cytokine levels, inhibited the growth of periodontitis-associated bacteria, and demonstrated pro-osteogenic properties. **Conclusion**: This study highlights the potential of Ce-ZIF-62 materials in modulating inflammatory responses in periodontal disease. These findings offer valuable insights into the development of functional materials for periodontal tissue regeneration, presenting significant implications for periodontal therapy.

References:

1. Garaicoa‐Pazmino C, Fretwurst T, Squarize CH, Berglundh T, Giannobile WV, Larsson L, et al. Characterization of macrophage polarization in periodontal disease. Journal of clinical periodontology. 2019;46(8):830-9.
2. Liu X, He X, Jin D, Wu S, Wang H, Yin M, et al. A biodegradable multifunctional nanofibrous membrane for periodontal tissue regeneration. Acta Biomaterialia. 2020;108:207-22.
3. Wu Y, Ta HT. Different approaches to synthesising cerium oxide nanoparticles and their corresponding physical characteristics, and ROS scavenging and anti-inflammatory capabilities. Journal of Materials Chemistry B. 2021;9(36):7291-301.

The sensory nerve regulates stem cell homeostasis through Wnt5a signaling

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Abstract:

Increasing evidence indicates that nerves play a significant role in regulating stem cell homeostasis and developmental processes. To explore the impact of nerves on epithelial stem cell homeostasis during tooth development, the regulation of sensory nerves on stem cell homeostasis was investigated using a rat model of incisor development. Impaired mineralization, decreased enamel thickness, and fractured enamel rods of the incisor were observed after denervation. qPCR and histological staining revealed that the expression of enamel-related factors ameloblastin (AMBN), kallikrein-4, amelogenin (Amelx), collagen type XVII (col17a), and enamelin were decreased in the incisor enamel of rats with sensory nerve injure. The decreased expression of Wnt5a in ameloblasts was coupled with the downregulation of calcium ion-related calmodulin kinase II. Furthermore, knockdown of Wnt5a in ALC cells significantly decreased the expression of enamel-related Amelx and Klk4. And the expression of bone-related genes and proteins such as RUNX2, ALP, and OPN decreased, and ALP staining also demonstrated a decrease in expression after knockdown of Wnt5a.These results implicate that the sensory nerves are essential in stem cell homeostasis for enamel mineralization and development. This provides new insights into the mechanism of neural influence on stem cell homeostasis, and may potentially contribute to future tooth regeneration.

Single-Atom Catalysts Regulate Aging Bone Homeostasis by Modulating Senescent Macrophages

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Abstract:
Age-related bone loss presents a significant healthcare challenge, with immunosenescence and dysregulated macrophage function playing crucial roles in compromised bone homeostasis. This study investigates the therapeutic potential of single-atom catalysts (SACs) in modulating senescent macrophage function to enhance bone regeneration in aging. We developed iron-based SACs with atomically dispersed metal centers on a zeolitic imidazolate framework, demonstrating exceptional efficiency in regulating reactive oxygen species (ROS) and cellular metabolism at concentrations below 10 μg/mL. In vitro studies using LPS-induced senescent THP-1 macrophages revealed that SAC treatment significantly reduced senescence markers, including SA-β-Gal expression and SASP-associated factors (IL-6, TNF-α, IL-1β). Metabolic analysis showed SAC treatment effectively protect macrophages from oxidative stress. Conditioned medium from SAC-treated senescent macrophages enhanced pro-regenerative properties, promoting vascularization and osteogenic differentiation in vitro. In aged rat models, local administration of SACs significantly improved bone regeneration and reduced age-related bone resorption, as evidenced by micro-CT analysis showing an increase in bone volume compared to controls. Mechanistic investigations revealed that SACs modulate key signaling pathways involved in macrophage polarization, particularly through NF-κB and NRF-2 pathways, thereby promoting an anti-inflammatory, pro-regenerative phenotype. This study presents a novel therapeutic approach using SACs to target age-related bone loss through immunomodulation of senescent macrophages, offering promising potential for treating aging-associated bone disorders.

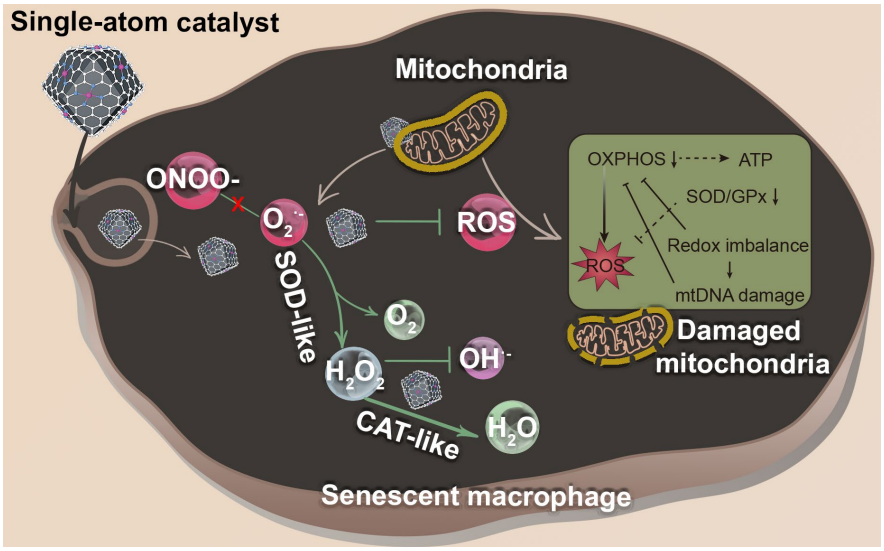

Figure 1. Schematic illustration of SACs in treating senescent macropahges

Ultrasound-Driven Radical Chain Reaction and Immunoregulation of Piezoelectric-Based Hybrid Coating for Treating Implant Infection

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Abstract:

The poor efficiency of US-responsive coatings on implants restricts its practical application. Immunotherapy that stimulates immune cells to enhance their antibacterial activity is expected to synergize with sonodynamic therapy for treating implant infection effectively and safely. Herein, US-responsive hybrid coating composed of the oxygen-deficient $BaTiO_3$ nanorod array and L-arginine ($BaTiO_{3-x}$/LA) on titanium implant for sonocatalytic therapy-cooperated immunotherapy is designed to treat Methicillin-resistant *Staphylococcus aureus* (MRSA) infection. $BaTiO_{3-x}$/LA can generate more oxidizing reactive oxygen species (ROS, hydroxyl radical (• OH)) and reactive nitrogen species (RNS, peroxynitrite anion ($ONOO^-$)). The construction of nanorod arrays and oxygen defects balances the piezoelectric properties and sonocatalytic capability under US. The generated piezoelectric electric field provides sufficient driving force for the separation of electrons and holes, and the oxygen defects attenuate the electron-hole recombination efficiency, consequently increasing the yield of ROS during the US treatment. Moreover, the released nitric oxide (NO) by L-arginine under US can react with superoxide radical (• O_2^-) to produce $ONOO^-$. This radical chain reaction improves the oxidizing ability between bacteria and radical. This process destroys the cell membrane (argB, secA2) and DNA (dnaBGXN), and the bacterial self-repair mechanism indirectly accelerates bacterial death based on the result of transcriptome analysis. In addition to participating in the radical chain reaction, NO also positively affects macrophage M1 polarization to display potent phagocytosis to MRSA. As a result, without introducing an extra sonosensitizer, $BaTiO_{3-x}$/LA exhibits excellent antibacterial activity against MRSA after the US treatment for 15 minutes. Furthermore, $BaTiO_{3-x}$/LA facilitates macrophage M2 polarization in the later stage after implantation and improves osteogenic differentiation. The combined effects of sonodynamic therapy and immunoregulation lead to an effective and safe treatment method for implant-associated infections.

Optimizing the bio-degradability and biocompatibility of a biogenic collagen membrane through cross-linking and zinc-doped hydroxyapatite

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Abstract:

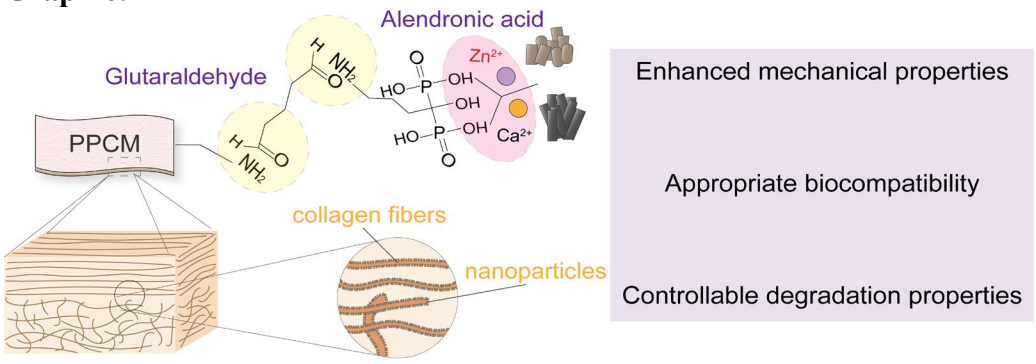
Objectives: Biogenic collagen membranes have been widely used as soft tissue barriers in guided bone regeneration (GBR). Nevertheless, their clinical performance remains unsatisfactory because of their low mechanical strength and fast degradation rate in vivo. As a fundamental nutritional trace element, zinc plays an active role in promoting the growth of cells and regulating the degradation of the collagen matrix. Herein, a biogenic collagen membrane was cross-linked with glutaraldehyde-alendronate to enhanced the mechanical properties and prolong degradation time.

Methods: In this study, nano-hydroxyapatite containing different concentrations of zinc ions (nZnHA) was prepared by chemical precipitation method, and biogenic collagen membrane (PPCM) was prepared using porcine peritoneum, and nZnHA-doped biogenic collagen membrane was prepared by crosslinking glutaraldehyde and alendronic acid. The mechanical properties, biocompatibility and degradation properties of the collagen membrane were studied in vivo and in vitro.

Results: The fabricated nZnHA-PPCMs not only retained the triple-helical structure of collagen fibers and the native three-dimensional network, but also possessed improved mechanical strength, a satisfactory biodegradation rate, appropriate pH and swelling rate, and capacity for continuous zinc release. In particular, 1% and 2% nZnHA-PPCMs showed preferable biocompatibility and a stronger promotion effect on MNGC formation than nHA-PPCM and 4% nZnHA-PPCM both in vitro and in vivo.

Discussion and Conclusion: An approach combining GA-alendronate cross-linking and nZnHA doping was presented for the improvement of a porcine-peritoneum-derived collagen membrane (PPCM) with higher mechanical strength and a lower biodegradation rate. Hence, this is a promising strategy to improve the clinical performance of biogenic collagen membranes by GA-alendronate cross-linking together with the incorporation of nZnHA.

Graphic:



Improvement of the ageing resistance of composite resins by Zr-doped mesoporous silica spheres (Zr-MSS)

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Abstract:
Since the 1960s, light-cured dental resins have gradually replaced amalgam as the most commonly used dental caries treatment material in clinical practice due to their superior advantages of aesthetics, biocompatibility, and operability. However, the service life of them is limited, and one of the main reasons for the failure of resin-based restorations is stress fracture due to their insufficient mechanical strength. Great efforts have been devoted to improve the mechanical properties of dental resin composites, such as designing new monomer structures and tailoring the size, morphology and surface characterization of the fillers. Among these, the application of mesoporous silica fillers has attracted great attention because of their significant reinforcing effect on dental resins[1]. However, mesoporous silica could be easily degraded in wet environments, leading to the poor ageing resistance of the materials[2]. In the present study, we prepared Zr-doped mesoporous silica spheres (Zr-MSS) to improve the chemical stability of the particles. The effect of Zr-MSS fillers on the performance of dental resins was investigated. The results demonstrated that Zr-MSS significantly improved the mechanical stability of dental resins. Furthermore, the addition of Zr-MSS did not impair the light-curing performance and biocompatibility of the composite resins. Therefore, the prepared Zr-MSS could be potential functional fillers for dental composite resins.

References:
[1] S. Zhang, X. Wang, J. Yang, H. Chen, X. Jiang, Micromechanical interlocking structure at the filler/resin interface for dental composites: a review, INTERNATIONAL JOURNAL OF ORAL SCIENCE 15(1) (2023).
[2] H. Li, J. Huang, H. Zhang, R. Hang, Y. Wang, Preparation of Al-doped mesoporous silica spheres (Al-MSSs) for the improvement of mechanical properties and aging resistance of dental resin composites, JOURNAL OF THE MECHANICAL BEHAVIOR OF BIOMEDICAL MATERIALS 157 (2024).

Self-supplying hydrogen via micro-magnesium wire-reinforced collagen membrane (Col-MMW) for advanced guided bone regeneration (GBR) via osteoimmunomodulation

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Abstract:
Hydrogen (H_2), once overlooked in biology, is now recognized as a signaling gas with therapeutic potential in diverse medical fields, including infection, inflammation, and oxidative stress-related disorders. Its capacity to selectively neutralize cytotoxic hydroxyl radicals (·OH), which lack natural enzymatic detoxification, sets it apart as a potent antioxidant. Unlike conventional antioxidants, H_2 can readily diffuse into cellular organelles, including mitochondria, due to its small size and non-polarity. Despite its promising antioxidative and anti-inflammatory roles, the localized delivery of H_2 in bone tissue engineering has remained largely unexplored.

In this study, we developed a novel metal-phenolic network (MPN)-coated micro-magnesium wire-reinforced collagen membrane (Col-MMW) for guided bone regeneration. This biomaterial leverages the dual benefits of Mg^{2+} release for bone regeneration and in situ H_2 generation to modulate the microenvironment. Metallic magnesium not only enhances the mechanical stability of the membrane but also facilitates the simultaneous release of H_2 and Mg^{2+} through its natural degradation in physiological conditions. Our findings revealed that Col-MMW mitigated inflammation by promoting macrophage polarization through NRF-2 activation and NF-κB suppression, with contributions from both H_2 and Mg^{2+}. These anti-inflammatory effects were validated in vitro and in vivo. Furthermore, the osteoimmunomodulatory properties of Col-MMW significantly enhanced osteogenesis in pre-osteoblast MC3T3 cells, with results confirmed in an in vivo model.

This study establishes Col-MMW as a dual-functional biomaterial that uniquely integrates localized H_2 delivery with Mg^{2+} release, offering a transformative approach to reducing inflammation and promoting bone regeneration. The findings hold significant promise for advancing regenerative medicine and biomaterial innovation.

Hard materials surface adsorbed proteins mediate fibrin network formation to regulate human gingival fibroblast behaviors

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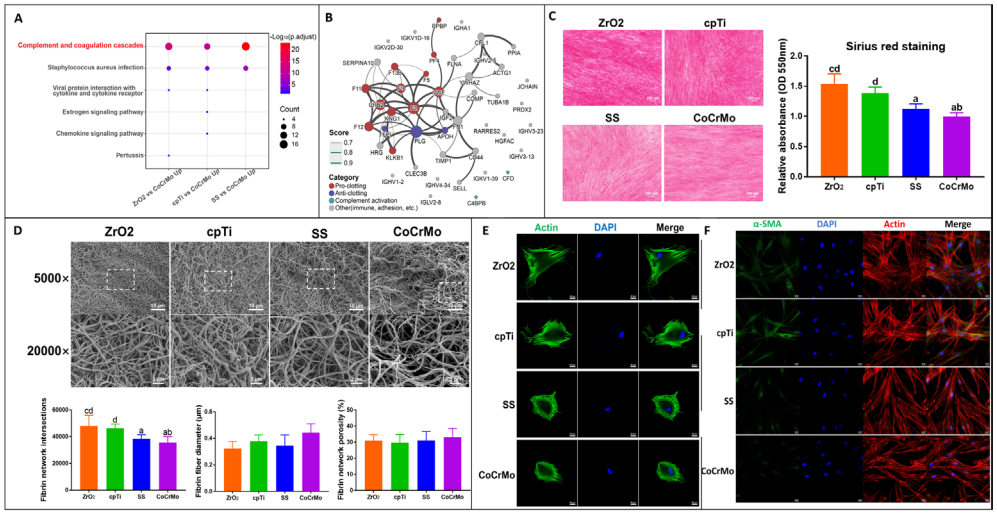
Abstract:
The integration between the hard materials and the gingival tissue around the transgingival portion is crucial for the success of the dental implant. Here, we decoded the adsorbed plasma protein profiles on four hard materials, zirconia (ZrO_2), Titanium (cpTi), cobalt-chromium-molybdenum (CoCrMo) and stainless steel (SS) by LC-MS/MS technique and bioinformatic approaches, which showed that their adsorbed protein profiles distinguished from each other. Specifically, compared to CoCrMo, the upregulated adsorbed proteins on ZrO_2, cpTi and SS were mainly related to enhancing the coagulating process, which consequently led to shorter clotting time of plasma and formation of denser fibrin network structures on them. By finite element analysis, it was showed that the denser fibrin protein network structure increased the contact area between cells and the fibrin network, which could have strong impacts on the integrin of human gingival fibroblast (HGF) cell and the downstream cellular reactions. By RNA-sequencing technique and bioinformatic approaches, it was indicated that this signal could affect the multiple behaviors of HGF cells including promoting the cell adhesion and activation. Correspondent experiments showed that HGF cells had better adhesion morphology and high expression of cell contraction and collagen synthesis-related genes and protein on the dense fibrin protein networks of ZrO_2, cpTi and SS when compared to CoCrMo. The results of this study should shed light into a novel strategy to improving the gingival attachment around dental implant by tuning materials surface properties to manipulate their adsorbed proteins hence to create a fibrin network which is suitable for gingival tissue cells to exert the integration function.

Graphics:



(A,B) Decoding the adsorbed protein profiles on four hard materials. (D) Fibrin network formed on the four groups. (C,E,F) Different biological responses of HGF in four groups.