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FC03.生命健康材料前沿国际论坛

分会主席: 张兴栋、王迎军、冷劲松、胡国华、Luigi Ambrosio、Dimitrios Angelis、王云兵 FC03-01

Silica Nanocarriers for Precision Drug Delivery

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Chemical processing of functional ceramics has played a key role in converging disciplines, which is especially true for biomedical applications. For example, the development of biocompatible drug-carriers that can hold back the payloads and release the drugs or antibiotics at the specific diseased area is a materials processing challenge. The selective transport and retention of drugs in sufficiently high concentrations at the target site is inhibited by various physiological barriers, which reduces or even blocks the therapeutic efficiency of molecular drugs. Therefore, advanced drug-delivery systems designed to overcome biological barriers are needed to meet the specific traits of physiological and disease-related barriers. In this context, chemically functionalized nanoparticles act as efficient drug-carriers to transport higher amounts of therapeutic payloads to diseased sites that also reduces the undesired off-site effects. Moreover, hollow nanocarriers can incorporate more than one drug enabling theranostic and theraregenerative approaches. Finally, ceramic nanoparticles can be modified with surface-bound target ligands to exploit the overexpression of receptors and promote cell specific attachment of the carriers for a localized high concentration of drug around disease sites. This talk will discuss the potential benefits of inorganic nanoparticles towards precision drug delivery,

FC03-02

Functional biomaterials for theragenerative medicine

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The implementation of a personalized therapy together a less invasive surgery for the restoration of human tissues is becoming an appropriate strategy to mitigate costs of the modern health care system and the maintenance of health and quality of life. The design biomaterials endowed with therapeutic and regenerative (theragenerative) properties are recently of particular interest [1]. The selection of a suitable injectable technique is often based on material characteristics (including mechanical properties, drug release kinetics and degradation) that serve for the specific treatment function. Micro or nano-structured materials in the form of gels, nanoparticles and nanocomposites have gained increasing interest in regenerative medicine because they are able to mimic the physical features of natural extracellular matrix (ECM) at the sub-micro and nano-scale levels and with the possibility to be bioactivated by bioactive compounds as naturally-derived eumelanin. Indeed, materials composed of gellan gum hydrogel and eumelanin displayed greater stability due to the presence of negatively charged groups along the eumelanin backbone [2]. 2D materials such as graphene oxide (GO) and exfoliated black phosphorus

(2D BP) show important therapeutic and regenerative activities due to their physicochemical properties. Recent studies have shown the effectiveness of 2D BP and GO as photodynamic therapy (PDT) agents for cancer treatment. This activity has been ascribed to their capability of generating singlet oxygen and acting as photosensitizers that, in presence of reactive oxygen species (ROS) and infrared light irradiation, constitute an essential component of PDT therapy [3]. On the other hand, the oxygen-containing functional groups of GO and the phosphates ions (PO₄³⁻) derived by BP decomposition act as anionic ligands for positive calcium ions (Ca²⁺), enhancing the attraction, binding, and aggregation of free Ca²⁺ in bone tissue, ultimately leading to the formation of calcium phosphate (CaP). In this way, GO and 2D BP represent bioactive signals able to promote osteogenesis [4,5]. Here, we propose the *in vitro* use of 2D substrates (GO and 2D BP) to inhibit cancer cell proliferation and migration and at the same time to preserve the healthy cells [6]. Furthermore, we offer an overview of how these 2D materials may be used to develop nanostructured hybrid materials (*e.g.*, gels, nanoparticles) as a theraregenerative platform for bone tissue engineering in terms of bone cancer therapy and regeneration.

Acknowledgements

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FC03-03

Phage-Based Biomaterials

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Bacteriophages, also called phages, are human-safe non-toxic viruses that specifically infect bacteria. They are one of the most common and diverse entities in biospheres. They can be pictured as nanobiomaterials assembled from proteins and nucleic acids. For example, filamentous phage (such as M13 phage) is a nanofiber (about 1 mm long and 7 nm wide) with multiple genetically modifiable proteins constituting a capsid and a DNA as a core inside the capsid. Therefore, they are ideal for many applications in precision nanomedicine and regenerative medicine. This talk will summarize my group's recent studies on the use of phages in these areas, including ultrasensitive biomarker detection for disease diagnosis, targeted drug delivery, directed stem cell differentiation, accelerated tissue formation, and nano-therapeutics for targeted disease treatment.

FC03-04

Flexible 3D neural bioelectronics and applications

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This presentation explores the development and applications of flexible 3D neural bioelectronics. Beginning with a comprehensive finite deformation theory that elucidates the climbing habits of twining plants, we establish fundamental insights into their attachment mechanisms. Leveraging this understanding, we propose a 3D twining electrode that can naturally self-climb onto nerves driven by 37 °C normal saline from a temporarily flattened 2D configuration. In vivo experiments demonstrate its potential for peripheral nerve stimulation and recording in neuroscience. Extending these principles, we introduce twining-inspired in-ear bioelectronics, named SpiralE. Utilizing electrothermal actuation, SpiralE adaptively expands and spirals along the auditory meatus, ensuring conformal contact while facilitating communication with the outside world. Visual and auditory Brain-Computer Interface (BCI) paradigms confirm that SpiralE achieves reliable EEG sensing, supporting wearable and discreet BCI control. Additionally, we present multifunctional bioelectronics with switchable rigidity and reconfigurable shapes, enabled by a fast thermal response shape memory polymer substrate. Taking advantage of its ability to be implanted through a small incision and recover in limited spaces to envelop biosurfaces, animal experiments demonstrate its efficiency in the comprehensive diagnosis of epilepsy and pericardial effusion. Furthermore, this presentation covers the development of magnetic resonance-compatible electrodes based on conductive polymers and stretchable multilevel mesh electrodes, discussing their applications in clinical brain diseases such as epilepsy and brain tumors. Overall, the development of flexible 3D neural bioelectronics, with their excellent biocompatibility, high robustness in modality fusion, and strong environmental adaptability, heralds a new generation of bio-electronic hybrid systems, driving innovation in advanced intelligence.

FC03-05

Cardiovascular materials and devices with tissue repair/regeneration function

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Cardiovascular diseases have become the leading cause of death worldwide. Safe and efficient treatment is critical which strongly relies on the utilization of implantable cardiovascular devices and relevant materials, including vascular stents, artificial heart valves, cardiac occluders, vascular grafts and injectable hydrogels for heart failure. This talk will focus on the advanced techniques in implantable cardiovascular materials and devices, especially the innovative ones developed in my lab in recent 10 years, including the first fully bioresorbable cardiac occluder approved by the regulatory body in the world in 2022 for the treatment of congenital heart disease, the first self-expanding pulmonary valve replacement system (VenusP-Valve®) with CE and NMPA approval in 2022, and the first minimally invasive interventional transcatheter hydrogel injection system in clinic in 2021 for the treatment of heart failure. Advanced techniques in this talk are focused on developing synthetic and natural materials with good biocompatibility, tunable biodegradability, enhanced tissue repair capacity, and functional coatings that can provide anti-coagulation, anti-calcification, anti-inflammation, and anti-infection performance. Representative findings include: 1) tailored design and discovery of recombinant humanized type III collagen that endows cardiovascular devices not only the promoted endothelialization but also anti-coagulation

ability; 2) novel double bond cross-linking technique for bioprosthetic heart valves (BHVs) with enhanced anti-calcification and endothelialization; 3) multifunctional coatings that mimic endothelial cell function, cell membranes or extra cellular matrix for cardiovascular tissue repair/regeneration. These findings also belong to the demonstration and discovery of tissue inducing materials in cardiovascular aspects. To access better cardiovascular materials and devices, further investigation of the following principles is needed: 1) cardiovascular materials with improved tissue-regeneration function; 2) development of intelligent interventional transcatheter medical devices; and 3) smart/precise techniques to address more solutions for patients.

FC03-06

工程化心肌组织的仿生构建和心脏再生研究

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Ischemic heart disease is one of the leading causes of death worldwide, with high clinical incidence and mortality rate. Tissue engineering strategies based on nanomaterials and stem cells provide a new treatment for repairing damaged myocardium. Based on this, our team has conducted a series of in vitro construction and myocardial infarction(MI) repair studies, systematically elucidating the fundamental principles of material regulation in myocardial development and remodeling, opening up a new approach to myocardial tissue construction and MI treatment based on conductive materials. A new strategy for cardiac regeneration based on microenvironment conditioning materials is proposed. This includes: 1) conducting key research on the construction of engineered cardiac tissue using natural extracellular matrix materials, elucidating the rules of biomaterial regulation of cell differentiation, dedifferentiation, and transdifferentiation. 2) Conducting research on the construction of cardiac patches and MI repair using novel conductive materials such as carbon-based materials, conductive polymers, and ionic conduction, revealing the basic rules of conductive nanomaterial regulation of myocardial cell development and assembly, improving the effectiveness of conductive ECTs in treating MI. 3) Combining the early inflammation, necrosis, ischemia, and other microenvironmental characteristics of MI, developing intelligent, actively self-regulating hydrogel scaffolds with anti-inflammatory, antioxidant, and pro-angiogenic effects. Through the targeted and on-demand delivery of functional nanoparticles and plasmids, effective control of inflammation, oxidation, angiogenesis, and electrical stimulation in the MI microenvironment has been achieved, greatly enhancing the regenerative repair capacity of the heart. In the future, biomimetic scaffolds with active microenvironmental regulation functions will play an important role in myocardial construction and cardiac regeneration.

FC03-07

硒纳米药物的肿瘤精准增敏与临床转化探索

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将围绕肿瘤放疗中的关键科学问题,以及如何解决放疗毒性、放疗耐受和免疫抑制三大瓶颈,开展创新型硒纳米药物(SeNPs)的研究。我们根据肿瘤的生化特点,设计具有靶向性的 SeNPs,实现精准给药,减少毒副作用。同时构建了具有肿瘤微环境响应特性的精确控释 SeNPs 用于克服肿瘤抑制瓶颈,提高肿瘤放疗敏感性和逆转放疗耐受。此外,我们还探索了通过 SeNPs 调节硒蛋白活性来激活自然/过继免疫系统的

放射/免疫协同治疗策略与临床转化应用,并揭示其逆转放疗诱导的免疫抑制的分子机制。

FC03-08

4D 打印形状记忆聚合物复合材料结构设计及其验证

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形状记忆聚合物作为一种典型的智能软材料,在特定的外界激励下(如热、电、光、磁等)能够从预先设定的临时形状回复到初始形状,在航天航空、生物医学、智能仿生、微机械工程等领域具有广泛应用前景。报告人基于形状记忆聚合物复合材料设计了构型、力学性能可调节、可重构的 4D 打印拉胀力学超材料和像素力学超材料,提出了匹配多种生物组织力学性能的超材料设计方法,验证了其力学性能和展开功能,设计了个性化定制且生物降解的 4D 打印形状记忆封堵器、肠道支架等,在生物医学领域进行了初步验证。

FC03-09

Poly(2-Oxazoline)-Based Functional Peptide Mimics Displaying Potent Antimicrobial Properties Runhui Liu*

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Microbial infections have long been associated with humans and are widespread worldwide. In recent years, drug-resistant bacteria, including "superbugs" and even multi-drug-resistant bacteria, have been rapidly emerging in clinical practice. This situation is very serious and is a great challenge for all mankind. Human beings are about to face the "post-antibiotic era" in which drug-resistant bacterial infections are not treatable. It is urgent and challenging to develop new antimicrobial agents that are highly effective and less susceptible to the emergence of microbial resistance.

Host defense peptides (HDPs) present in a wide range of living organisms have broad-spectrum antimicrobial activity and immunomodulatory functions, and are part of the natural protective barrier and innate immune process of living organisms. Therefore, HDP as a novel antimicrobial agent is highly expected in the research and solving the problem of microbial drug resistance. However, its drawbacks such as intolerance to enzymatic degradation, expensive price, and difficult to prepare in large quantities limit the practical application. We mimic some important biological functions of natural peptides by amino acid polymers and study the related mechanisms and applications. By introducing non-natural amino acids, the prominent drawback of natural peptides that are easily hydrolyzed by proteases can be targeted. We have discovered amino acid polymers that promote osteoblast adhesion comparable to the gold standard RGD peptide for cell adhesion, and the amino acid polymers show desirable bone damage repair functions and applications.

In the second part, we found that poly(2-oxazoline) can be used as a new class of peptide mimics to mimic HDP to obtain excellent antimicrobial activity. We successively found that the optimal poly(2-oxazoline) could have efficient activity against drug-resistant bacteria and drug-resistant fungi. The optimal poly(2-oxazoline)s are comparable to, or even superior to, the activity of the control antimicrobial drugs. They also have good biosafety and have not been found to cause resistance problems in bacteria and fungi with continuous use. The effective in vivo antibacterial and antifungal function, especially for the treatment of systemic and invasive infections, was also verified in animal in vivo experiments. These studies indicate that HDP-mimicking poly(2-oxazoline)s have a

wide range of applications in the field of antimicrobial drugs and biomaterials.

FC03-10

E-cardiac patch to sense and repair infarcted myocardium

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Conductive cardiac patches can rebuild the electroactive microenvironment for the infarcted myocardium but their repair effects benefit by carried seed cells or drugs. The key to success is the effective integration of electrical stimulation with the microenvironment created by conductive cardiac patches. Besides, due to the concerns in a high re-admission ratio of heart patients, a remote medicine device will underpin the successful repair. Herein, we report a miniature self-powered biomimetic trinity triboelectric nanogenerator with a unique double-spacer structure that unifies energy harvesting, therapeutics, and diagnosis in one cardiac patch. Trinity triboelectric nanogenerator conductive cardiac patches improve the electroactivity of the infarcted heart and can also wirelessly monitor electrocardiosignal to a mobile device for diagnosis. RNA sequencing analysis from rat hearts reveals that this trinity cardiac patches mainly regulates cardiac muscle contraction-, energy metabolism-, and vascular regulation-related mRNA expressions in vivo. The research is spawning a device that truly integrates an electrical stimulation of a functional heart patch and self-powered e-care remote diagnostic sensor.

FC03-11

Biomimetic coatings for blood-contacting materials

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The development of biomimetic technology opens up the possibility of building biomaterials with better performance. The study focused on the response characteristics between the material/blood and materials/tissue, developed the tailored biomimetic coating strategy for blood-contacting materials. Briefly, coatings that can mimic cell-membrane, extracellular matrix and endothelial function were designed and performed on different blood-contacting devices. This talk will also consider the scientific issues behind the difficulty of current surface-functionalized modification techniques. Engineered cell membrane were developed to coat macroscale materials with complex shape to realize a direct succession of the cell membrane platform with both anti-fouling and membrane protein mediated interaction ability which can be considered as an ideal mimicking to modify blood-contacting materials and devices.

FC03-12

Peripheral Nerve Injury and Regenerative Microenvironment

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Neuronal microenvironment imbalance is associated with successive and irreversible pathophysiological changes and insufficient functional restoration after peripheral nerve injury. Conventional neural-supporting

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

FC03-13

微环境响应水凝胶用于心脑血管疾病治疗

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心脑血管疾病已经成为国民健康的第一杀手,远高于肿瘤、呼吸疾病,成为首位致死原因,占居民疾病死亡比 45%以上。目前,中国心脑血管疾病患者已达 3.3 亿,常见心脑血管疾病包括冠心病、心脏瓣膜疾病、心力衰竭、先天性心脏病、脑梗等。心脑血管疾病常常表现出四高一多的特点,发病率高、死亡率高、致残率高、复发率高及并发症多等特点,其中心力衰竭和脑梗是最具代表性的两种疾病,其治疗仍然是心脑血管治疗领域尚未突破的巨大挑战。近年来,相关研究已证实微环境响应水凝胶在治疗心衰和脑梗方面的安全性和有效性。然而,当前的水凝胶治疗策略研究往往针对梗死区域微环境中的一部分因素展开,无法有效应对心梗区域复杂的微环境且无法满足受损心脑组织修复多阶段的不同需求,常常导致治疗效果不佳,尚存在一定局限性。针对以上问题,我们设计了一系列微环境响应水凝胶体系用于心衰和脑卒中的治疗,将梗死区域微环境看做一个整体进行突破,通过逐级调控受损心肌和脑组织的修复过程,从多维度重塑梗死微环境以达到最佳治疗效果。

FC03-14

Selectively suppressing tumor angiogenesis for targeted cancer therapy by genetically engineered phage Yan Li, Weilian Sun, Chuanbin Mao* Zhejiang University

Anti-angiogenesis is a promising approach to cancer therapy but is limited by the lack of tumor-homing capability of the current anti-angiogenic agents. Angiogenin, a protein over-expressed and secreted by tumors to trigger angiogenesis for their growth, has never been explored as an anti-angiogenic target in cancer therapy. Here we show that filamentous fd phage, as a biomolecular biocompatible nanofiber, can be engineered to become capable of first homing to orthotopic breast tumors and then capturing angiogenin to prevent tumor angiogenesis, resulting in targeted cancer therapy without side effects. The phage was genetically engineered to display many copies of an identified angiogenin-binding peptide on its side wall and multiple copies of a breast tumor-homing peptide at its tip. Since the tumor-homing peptide can be discovered and customized virtually towards any specific

cancer by phage display, the angiogenin-binding phages are thus universal "plug-and-play" tumor-homing cancer therapeutics.

FC03-15

Theranosties nanoplatform for photoacoustic diagnosis and multipath treatment of atherosclerosis

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Background and purpose: Atherosclerosis can cause severe cardiovascular disease, which is usually diagnosed in late stageswith life-threatening complications. Thus, timely diagnosis and effective treatment of early-stage atherosclerosis is a matter of vital importance to minimize the risk of cardiovascular disease.

Methods: A series of conjugated polymers was constituted as the probe for non-invasive photoacoustic diagnosis, while the rapeutic complexes were also prepared for treatment through the regulation to lipid distribution and immuno microenvironment. The probe and regulators were co-packaged into nanoparticles, which were further coated with targeting structure for active accumulation into the plaques.

Conclusions: During the blood circulation, the coating of nanoparticles provided a directional recognition to the atherosclerotic lesions. Subsequently, the local microenvironment in the pathological plaques could trigger the disassembly of nanoparticles, where the packaged probe and regulator were accurately delivered. The probe promised a distinct photoacoustic imaging to the atherosclerotic plaques without any invasion. At the same time, the regulator could transfer the cumulated lipid or rebuild the immunal microenvironment, which resulted in the restraint on atherosclerotic progression and the further reversal of formed lesions. The nanoplatforms we built delivered a compositive targeting, diagnosis, inhibition and degradation of early-stage atheroscleroticlesions through the active recognition, non-invasive photoacoustic diagnosis and regulation to the lipid distribution or immunoenvironment, which provides valuable ideas for the clinical risk management of early-stage atherosclerosis.

FC03-16

生物芯片的金纳米颗粒结构设计与合成

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纳米生物技术是纳米技术与生物技术的结合,其更多的意义在于:用纳米尺度下的材料、设备和手段推进生物学研究。反之,生物技术却有限地应用于新型纳米材料和技术的研发。本报告将探讨生物分子在光学功能材料的合成过程中所发挥的独一无二的精细调控能力。其中,核酸分子可在小于 5 纳米的尺度内控制金纳米颗粒的生长,这解决了金纳米结构无法在液相中设计性调控的技术问题。特定结构的等离子纳米材料与光相互作用可产生独特的等离子体共振效应,可推进高灵敏的生物分子检测技术和光催化等技术的创新发展,具有重要意义。

FC03-17

The study of the activation of epicardial cells in situ by functional nanomaterials to promote myocardial infarction repair

Chen Song,Leyu Wang,Xiaozhong Qiu* Southern Medical University

Restoring damaged myocardial tissue with therapeutic exogenous cells still has some limitations, such as immunological rejection, immature cardiac properties, risk of tumorigenicity, and a low cell survival rate in the

ischemic myocardium microenvironment. Activating the endogenous stem cells with functional biomaterials might overcome these limitations. Research has highlighted the multiple differentiation potential of epicardial cells via epithelial—mesenchymal transition (EMT) in both heart development and cardiac regeneration. In our previous research, a carboxylic gelatin—methacrylate (carbox-GelMA) nanoparticle (NP) was fabricated to carry ammonium persulfate (APS), and APS-loaded carbox-GelMA NPs (NPs/APS) could drive the EMT of MCF-7 cells in vitro and promote cancer cell migration and invasion in vivo. The present study explored the roles of functional NPs/APS in the EMT of Wilms' tumor 1- positive (WT1+) epicardial cells and in the repair of myocardial infarction (MI). The WT1+ epicardial cells transformed into endothelial-like cells after being treated with NPs/APS in vitro, and the cardiac functions were improved signiffcantly after injecting NPs/APS into the infarcted hearts in vivo. Furthermore, simultaneous activation of both autophagy and the mTOR pathway was conffrmed during the NPs/APS-induced EMT process in WT1+ epicardial cells. Together, this study highlights the function of NPs/APS in the repair of MI.

FC03-18

属-有机/无机杂化层改性锌金属促进骨质疏松性骨折修复

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引言:可降解锌金属在临床骨质疏松性骨折治疗具有光明的应用前景,其中锌金属具有比镁及铁基金属更适宜的降解速率、力学强度及锌离子潜在促成骨与抑制破骨的功能,被认为是理想的骨折修复用材料[1]。然而,锌金属降解不均匀、过量锌离子释放导致细胞毒性、成骨性能不足且不具备抑制破骨功能,限制了临床应用[2,3]。表面改性是解决以上问题的有效途径。基于此,本研究在锌金属表面制备一种微纳仿生的金属-有机纳米棒介导的磷酸锌杂化涂层,以改善锌金属降解并兼备成骨与破骨协同促骨质疏松性骨折修复功能。

材料与方法:基于化学配位螯合作用合成了锌-唑来膦酸/羟基乙叉二膦酸金属-有机纳米棒,并将纳米棒作为模板和形核位点原位诱导磷酸锌的形成。

结果与讨论:如图 1 所示,杂化涂层促进了活性钙磷盐的沉积、碱性磷酸酶的表达、钙结节的形成,显示出良好的促成骨性能。此外,改性锌金属可有效抑制破骨细胞增殖及分化。如图 2 所示,表面改性锌金属髓内钉在大鼠骨质疏松性骨折模型中表现出促进骨折愈合的功能,该研究不仅为可降解金属的表面改性提供了新的途径,而且对于更好的理解骨科用新型可降解生物材料有一定帮助。

FC03-19

Synergistic effect of hyaluronic acid and its derivatives with astaxanthin to improve the corrosion resistance and biocompatibility of ZE21B magnesium alloy surface

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Cerebrovascular and cardiovascular diseases have been a major threat to global public health over the years. Stent intervention is the most effective technique to overcome them. Magnesium (Mg) alloy is a promising material for cerebrovascular and cardiovascular stents and has been implemented in clinical practice owing to its outstanding mechanical properties. However, the excessive degradation rate and delayed surface endothelialization remain significant limitations to the further application of Mg alloy stents in cerebrovascular intervention. With this consideration, a multifunctional composite coating improved the surface modification of

Mg alloy. In this study, a multifunctional composite coating composed of hyaluronic acid (HA) and astaxanthin (ASTA) was applied to accelerate the surface endothelialization of Mg alloy. Additionally, it promotes smooth muscle cells (SMC) and endothelial cells (EC) and regulates macrophages to the M2 phenotype, all of which contribute to endothelialization. The results showed that the HA/ASTA composite coating has enhanced the corrosion resistance, biocompatibility, anti-inflammation, anti-hyperplasia, and anti-coagulation of the Mg alloy stent.

FC03-20

具有多种药物可控释放的电纺仿生骨膜实现程序化促骨再生

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The effective repair of large bone defects remains a major challenge due to its limited self-healing capacity. Inspired by the structure and function of the natural periosteum, an electrospun biomimetic periosteum is constructed to programmatically promote bone regeneration using natural bone healing mechanisms. The biomimetic periosteum is composed of a bilayer with an asymmetric structure in which an aligned electrospun poly(ε-caprolactone)/gelatin/deferoxamine (PCL/GEL/DFO) layer mimics the outer fibrous layer of the periosteum, while a random coaxial electrospun PCL/GEL/aspirin (ASP) shell and PCL/silicon nanoparticles (SiNPs) core layer mimics the inner cambial layer. The bilayer controls the release of ASP, DFO, and SiNPs to precisely regulate the inflammatory, angiogenic, and osteogenic phases of bone repair. The random coaxial inner layer can effectively antioxidize, promoting cell recruitment, proliferation, differentiation, and mineralization, while the aligned outer layer can promote angiogenesis and prevent fibroblast infiltration. In particular, different stages of bone repair are modulated in a rat skull defect model to achieve faster and better bone regeneration. The proposed biomimetic periosteum is expected to be a promising candidate for bone defect healing.

FC03-21

Strategy of in situ modification of controlled release polymer brush to construct high performance heart valve materials

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Minimally invasive heart valve replacement has gradually become the mainstream treatment for severe heart valve diseases[1]. Biological valves have become the first choice for constructing minimally invasive heart valves because of their superior hemodynamic performance and no need for long-term anticoagulation. However, currently commercial glutaraldehyde crosslinked biological valve materials still suffer several problems such as poor biocompatibility, calcification, coagulation, inflammation and limited durability[2]. The development of new type of crosslinking agents with better biocompatibility and easily regulated properties and functional modification strategies is expected to fundamentally overcome the inherent defects of glutaraldehyde crosslinked valves and obtain new biological valve materials with better comprehensive properties.

Based on the current situation that there is no relatively systematic non-glutaraldehyde biological valve construction and functional modification strategy, and the application prospect of in-situ polymer brush modification strategy based on oxazolidine crosslinked biological valve materials in improving the properties such as anti-calcification, anti-coagulation and anti-inflammatory, this project will design and develop a new bifunctional oxazolidine-based crosslinking agent that can induce controllable free-radical polymerization. A

series of biological valve materials with excellent comprehensive performance will be constructed by modifying the block polymer brush in situ on the biological valve materials with drug-controlled release function, which would effectively meet the multiple performance requirements of biological valves and provide a new direction for the research and development of high performance biological valve materials and other blood contact materials.

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FC03-22

基于硫化氢供体的抗炎促修复血管支架分子刷

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微创介入血管支架植入术已成为治疗冠心病的最有效手段之一,挽救了众多患者的生命。然而,晚期血栓和再狭窄仍然是限制血管支架临床疗效的两大主要并发症。硫化氢(H₂S)作为第三大内源性气体递质,在心血管系统中发挥重要的生物学作用,包括抗炎作用、保护线粒体功能、血管舒张以及减轻心血管系统的氧化应激。本研究利用二苯甲酮(BP)两步光引发聚合表面接枝技术,在血管支架表面构建含有H₂S 供体和 RGD 的生物活性分子刷。通过体外血液相容性和细胞实验,以及体内皮下植入和兔髂动脉植入实验,评价了该生物活性分子刷支架的生物学性能。血小板和体外动静脉分流实验表明,H₂S 有效提高了支架的血液相容性。体外细胞实验显示,H₂S 能够选择性促进内皮细胞(ECs)的粘附和增殖,同时抑制平滑肌细胞(SMCs)的粘附和增殖。H2S 显著抑制了巨噬细胞的粘附和活化,表现出良好的抗炎性能,这一发现也在皮下植入实验中得到进一步确认。兔髂动脉植入实验表明,H₂S 可有效降低支架植入后的炎症反应,加快了内皮化进程,并有效抑制了新生内膜的过度增生。该研究不仅证实了 H₂S 在血管支架改性方面的应用潜力,还为心血管材料与器械的设计提供了新思路。

FC03-23

Modular design of functional coatings with self-response to microenvironment for vascular stent

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Background and purpose:

Early coagulation and inflammation after implantation are complex and interconnected, which not only hinders the reendothelialization process but also affects the long-term performance of vascular stents. However, the influence mechanism of anti-coagulant and anti-inflammatory modification on reendothelialization, and the efficient strategy of combination and selection have yet to be explored. Taking the interaction between material and organization as the starting point, this project intends to construct a self-regulating coating with microenvironment adaptability by combining anti-coagulation and anti-inflammation.

Methods

Here, we constructed an anti-coagulant module with self-regulating ability by encapsulating apixaban in thrombin-triggered nanogels, crosslinked by thrombin-responsive peptide and oxidized-dextran. Epigallocatechin gallate (EGCG) was chosen as the anti-inflammatory module, as its regulatory of oxidative stress and inflammatory response. On the basis of ensuring the independence of these two modules, we combined them with a biocompatible crosslinked thin coating scaffold. Triggered by the high risk of coagulation response, the anti-coagulant module could inhibit multiple stages of the clotting response. The anti-inflammatory module could regulate the inflammation through multiple pathways. The coating interfered with adverse coagulant and

inflammatory responses, and provided a favorable environment with for subsequent reendothelialization. The design and performances of coating were investigated and optimized. The anticoagulant capacity, anti-inflammatory capacity and effects on cells were well verified.

Conclusions:

The coating exhibits ideal anti-platelet activation capacity, and interfered with platelet-macrophage interactions. Through eliminating free radicals and inhibiting macrophage activation, the coating regulated inflammatory response effectively. The multifunctional coating also promoted the growth of endothelial cells and inhibited the excessive proliferation of smooth muscle cells. Through the development of the project, the relationship between anti-coagulation and anti-inflammatory functions and their effects on reendothelialization were understood. This project provided experimental guidance and technical reserve for the design and optimization of surface modifications on vascular stent.

FC03-24

金属-有机/无机杂化功能层改性可降解锌用于骨修复

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引言: 锌及其合金具有中等的腐蚀速率、较好的机械性能和潜在的生物功能性,在骨植入体应用领域展现出巨大的潜力[1]。然而,局部或小孔腐蚀所致的提前断裂及力学性能失效、过量锌离子释放导致的细胞毒性和骨整合过程受损、促骨再生性能不足是亟待解决的关键问题,表面改性是关键[2,3]。本研究采用化学交替沉积法,在锌合金表面构建了兼具成血管-成骨耦合促骨再生和腐蚀调控的金属-有机/无机杂化涂层,加速了大鼠骨折/缺损的愈合。

材料与方法:利用金属离子与活性分子之间的螯合作用形成金属-有机纳米颗粒,并诱导无机相原位形核生长,形成金属-有机/无机杂化涂层。

结果与讨论: 杂化涂层具有成血管-成骨耦合促骨再生的潜力。在涂层的作用下,内皮细胞和干细胞之的旁分泌作用会增强,能够促进内皮细胞的迁移和成管以及干细胞分化。改性锌基髓内钉植入大鼠骨质疏松性股骨骨折 16 周后的 Micro CT 结果以及定量数据表明,相比于纯锌和 Ti6Al4V,改性的锌金属具有更好的促进骨愈合的能力。

结论: 金属-有机/无机杂化涂层调控了锌基底的腐蚀/降解行为,表现出成血管-成骨耦合促骨再生的功能,加速了大鼠骨质疏松性骨折的的愈合。

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FC03-25

仿生动态抗污表面改性临时性介入器械的研究

张文泰

Protein and cell adhesion on temporary intravascular devices can lead to thrombosis and tissue embedment, significantly increasing complications and device retrieval difficulties. Here, we propose an endothelial glycocalyx-inspired dynamic antifouling surface strategy for indwelling catheters and retrievable vascular filters to prevent thrombosis and suppress intimal embedment. This strategy is realized on the surfaces of substrates by the intensely dense grafting of hydrolyzable endothelial polysaccharide hyaluronic acid (HA), assisted by an amine-rich phenol-polyamine universal platform. The resultant super-hydrophilic surface exhibits potent antifouling property against proteins and cells. Additionally, the HA hydrolysis induces continuous degradation of the coating, enabling removal of inevitable biofouling on the surface. Moreover, the dense grafting of HA also ensures the medium-term effectiveness of this dynamic antifouling surface. The coated catheters maintain a superior anti-thrombosis capacity in ex vivo blood circulation after 30 days immersion. In the abdominal veins of rats, the coated implants show inhibitory effects on intimal embedment up to 2 months. Overall, we envision that this glycocalyx-inspired dynamic antifouling surface strategy could be a promising surface engineering technology for temporary intravascular devices.

FC03-26

A strongly robust chitosan-based hydrogel for adaptive repair of myocardial infarction

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The hydrogel-based engineered cardiac patch (ECP) holds great promise as a potential treatment option for myocardial infarction (MI). However, it remains a challenge to optimize the preparation of ECP integrated with biocompatibility, mechanical stability, and adaptation to the MI repair. Herein, we constructed chitosan (CS) hydrogel with good mechanical robustness through the template method to adapt to the continuous beating of myocardial tissue. On this basis, with the synergistic effects among lipoic acid (TA), proanthocyanidins (PAs), and Eu³⁺, a functional platform capable of improving mitochondrial function, antioxidation, and pro-vascularization had been further constructed for adaptive repair of the MI microenvironment. The fabricated functionalized chitosan hydrogel (CS/TA@PAs-Eu) possessed good mechanical stability and ionic conductivity, showing potential for long-term adaptation to myocardial tissue pulsation. Also, the CS/TA@PAs-Eu hydrogel promoted cardiomyocytes (CMs) maturation and functionalization, and effectively improved mitochondrial function, scavenged reactive oxygen species (ROS) as well as promoted angiogenesis. The animal studies indicated that the CS/TA@PAs-Eu hydrogel could perform adaptive repair of MI to prevent left ventricular remodeling and restore cardiac function. This study highlighted a functionalized hydrogel ECP with good biocompatibility and mechanical robustness for the adaptive repair of MI.

FC03-27

生物瓣膜交联和功能化改性研究进展

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引言:随着人口老龄化加剧心脏瓣膜疾病患病率逐渐上升。进行人工心脏瓣膜置换有利于挽救患者生命。由于流体力学性能优越及可微创植入的特点,生物瓣膜逐步获得患者的认可。临床使用的生物瓣膜均由戊二醛交联。然而戊二醛交联生物瓣膜仍存在细胞相容性差、钙化、炎症反应和结构性破坏等问题,严

重影响其使用年限[1]。发展一种新型交联剂作为戊二醛替代物具有重要研究价值。我们以甲基丙烯酸异氰基乙酯为交联剂,探索了甲基丙烯酸异氰基乙酯交联瓣膜的稳定性、细胞毒性、机械性能、抗钙化性能、流体力学性能和耐久性。

材料与方法:以脱细胞猪心包膜(PP)为瓣膜材料,将 PP 浸泡于甲基丙烯酸异氰基乙酯(ICM)交联剂溶液中处理 24h,再用过硫酸铵/亚硫酸氢钠溶液引发聚合反应 24h 得到甲基丙烯酸异氰基乙酯交联的猪心包膜(PICM-PP)。对所得 PICM-PP 进行酶降解实验、细胞毒性、内皮细胞生长、单轴拉伸、大鼠皮下植入实验并与戊二醛交联猪心包膜(GA-PP)作对比。最后根据 ISO5840-3 的测试指导意见通过脉动流和加速疲劳试评估 PICM-PP 的流体力学性能和耐久性。

结果与讨论:由于不存在毒性残留醛基及游离于瓣膜材料上的戊二醛,PICM-PP 无明显细胞毒性,有利于内皮细胞增殖。异氰酸酯基团与氨基等基团的化学反应活性较高[2],因而交联度增高,使得瓣膜稳定性和机械性能得到提升。对植入后的材料进行免疫分析发现,PICM-PP 周围的免疫细胞较少,显示出较低的炎症反应。此外,大鼠皮下植入 30 和 90 天后钙化程度远低于 GA-PP 组。脉动流和加速疲劳实验结果显示,PICM-PP 已完成 2.5 亿次循环且结构完整、功能正常,满足 ISO5840-3 对生物瓣膜的流体力学性能和耐久性的要求。

结论:甲基丙烯酸异氰基乙酯交联的猪心包膜细胞相容性好,稳定性高,免疫反应低,钙化程度低,流体力学性能和耐久性符合 ISO5840-3 对生物瓣膜的要求。甲基丙烯酸异氰基乙酯是一种具有应用潜力的新型非戊二醛交联剂。

FC03-28

开发具有抗氧化活性的可注射水凝胶用于治疗年龄相关性黄斑变性

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累积的氧化损伤可能导致不可逆的视网膜色素上皮(RPE)细胞死亡,是干性年龄相关性黄斑变性(AMD)的主要原因,常导致老年人失明。本研究设计了一种由氧化的 HA(OHA)和己二酸二酰肼修饰的 HA(HA-ADH)组成的可注射水凝胶,用于递送抗氧化药物杨梅素(MY)。为提高药物的溶解性,利用羟丙基-β-环糊精进行包裹。流变学结果表明(负载 MY 的水凝胶(H-MY)的储能模量约为 202 Pa,具有良好的自愈合性能。此外,水凝胶具有多孔结构,和快速的体外酶降解性能,并在体外持续释放 MY 两周。

首先,我们考察了水凝胶对稳定自由基 DPPH、氢氧根和超氧根的清除效率。结果如图 11A 和 B 所示,H-MY 对这三种自由基的清除效率都超过 60%,表明该材料具有一定的抗氧化活性。其次,我们用碘酸钠处理 RPE 细胞,体外构建了细胞的氧化应激模型。DCFH 荧光染色和流式结果表明,相比于碘酸钠和空白水凝胶 (H-C) 组,H-MY 可以有效减少细胞内 ROS 的水平,这进一步证明了材料的抗氧化活性。同时,H-MY 可有效减少碘酸钠导致的细胞线粒体损伤和减少细胞凋亡水平。鉴于 H-MY 具有良好的抗氧化效果和细胞保护作用,我们进一步验证了其作为 AMD 体内治疗制剂的潜力。使用腹腔注射碘酸钠的小鼠作为AMD 模型,水凝胶经玻璃体内注射。碘酸钠组的小鼠眼底图像似乎比 PBS 组更亮,并显示斑点,H-MY 组的小鼠视网膜与 PBS 组(正常组)接近,没有观察到明显的地理萎缩迹象。为了进一步评估视网膜的生理功能,我们利用光学相干断层扫描(OCT)观察了小鼠的视网膜。OCT 图像显示,碘酸钠注射会使整个视网膜层变薄,并导致视网膜结构紊乱,表明碘酸钠组的小鼠存在严重视网膜损伤,而 H-MY 可以有效减少碘酸钠诱导的视网膜损伤。通过视网膜电图(ERG)检查视网膜的暗视反应。碘酸钠注射后,A 波和 B 波的振幅均显著降低,表明氧化损伤导致光感受器和双极细胞功能障碍。然而,H-MY 组的小鼠在 A 波和 B 波的振幅上对光刺激表现出相对较好的反应。ZO-1 染色结果显示,碘酸钠组的小鼠视网膜出现严重的 RPE 层畸形,细胞完整性和紧密连接被严重破坏;而 H-MY 组的视网膜显示出比较完整的多边形 RPE 细胞结构。结合上述结果,H-MY 可以有效减少碘酸钠导致的视网膜损伤,保护其生理功能。因此,这种可

注射抗氧化可注射水凝胶有望成为治疗 AMD 的"新武器"。

FC03-29

Anti-fouling Plus: A ROS-Triggered Coating Strategy with On-Demand Regulation of Inflammation to Favor Tissue Healing on Vascular Devices

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Cardiovascular diseases (CVDs) stand as the primary cause of death and a significant contributor to global disability. Cardiovascular stents, which involve guided balloon dilation at the site of stenosis, are widely recognized as the highly efficient therapies for coronary artery disease. Unhealthy vascular tissue healing after stenting is primarily triggered by endothelial dysfunction and excessive smooth muscle cell proliferation, which is induced and aggravated by local thrombosis and excessive inflammation. Excessive inflammatory response is closely related to elevated concentrations of reactive oxygen species (ROS). Here, an environment-friendly coating strategy termed "Anti-fouling plus" with inflammatory self-regulation ability was proposed. Upon this, membrane-mimicking copolymer MA(PCLA) served as the antifouling coating, effectively inhibiting coagulation and inflammation during the early stage of implantation. Furthermore, a ROS-responsive prodrug was drawn into the coating to promote tissue healing. A molecular prodrug of thioketal-bearing dexamethasone was engineered to be released in a controlled and responsive manner in response to externally high levels of ROS. The released dexamethasone exhibited highly effective anti-inflammation properties after implantation. The combination of ROS-responsive prodrug and membrane-mimicking antifouling interface strategy intelligently integrated inflammation responsiveness and regulation, which could mediate a gentle vascular microenvironment and thus promote vascular remodeling. In vitro tests revealed that the "Anti-fouling plus" coating could effectively impede protein adhesion while concurrently exhibiting anticoagulant and anti-inflammatory characteristics. In vivo stent implantation studies demonstrated that the proposed "Anti-fouling plus" coating effectively inhibited neointima hyperplasia, modulated the inflammatory response, and promoted endothelialization, offering promising surface modification approaches for vascular stents. In general, the novel stent coating approach that simultaneously integrated the feature of nanomedicine and cardiovascular interventions could modulate the intravascular microenvironment and mediate tissue healing, providing a new perspective on prognosis following stent implantation and offering a new solution for clinical translation.

墙报

FC03-P01

A probe for NIR-II imaging and multimodal analysis of early Alzheimer's disease by targeting CTGF

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Alzheimer's disease (AD) is the most prevalent neurodegenerative disease. Accurate early diagnosis of AD permits timely intervention, thereby delays AD progression. To date, earlier diagnosis of Alzheimer's disease (AD) is still challenging. Recent studies revealed the elevated expression of connective tissue growth factor (CTGF) in AD brain is an upstream regulator of amyloid-beta ($A\beta$) plaque, thus CTGF could be an earlier diagnostic

biomarker of AD than $A\beta$ plaque. Herein, we develop a peptide-coated gold nanocluster that specifically targets CTGF with high affinity (KD ~ 21.9 nM). The probe can well penetrate the blood- brain- barrier (BBB) of APP/PS1 transgenic mice at early-stage (earlier than 3-month-old) in vivo, allowing non-invasive NIR-II imaging of CTGF when there is no appearance of $A\beta$ plaque deposition. Notably, this probe can also be applied to measuring CTGF on postmortem brain sections by multimodal analysis, including fluorescence imaging, peroxidase-like chromogenic imaging, and ICP-MS quantitation, which enables distinguishment between the brains of AD patients and healthy people. This probe possesses great potential for precise diagnosis of earlier AD before $A\beta$ plaque formation.

FC03-P02

生物瓣膜的双键化以及表面修饰研究

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引言:瓣膜性心脏病是一种多发于老年群体且致死率较高的疾病,使用人工心脏瓣膜置换病变心脏瓣膜是治疗瓣膜性心脏病的金标准。生物瓣由于具有适宜的血流动力学性能和更低的致栓性得到广泛认可。然而传统戊二醛交联生物瓣存在的钙化、血栓以及细胞毒性等缺陷会缩短其使用寿命[1]。设计一种生物瓣改性策略具有很大的研究意义以及商业价值。我们开展了一种基于戊二醛的共交联以及后修饰策略对心包材料进行改性,并围绕抗钙化性能、血液相容性以及细胞相容性等方面对其进行表征与探究。

材料与方法:以脱细胞猪心包膜(PP)为瓣膜材料,将 PP 浸泡于 2-氨基-4-戊烯酸(APA)溶液中 12h,再加入戊二醛溶液,并持续摇晃 24 h 得到 2-氨基-4-戊烯酸共交联的心包(APA-PP)。然后将 APA-PP 浸泡于甲基丙烯酸 2-羟乙酯(HEMA)溶液中 12h,最后加入过硫酸铵以及亚硫酸氢钠引发自由基聚合反应,得到聚甲基丙烯酸 2-羟乙酯接枝的心包材料(HEMA-PP)。对 HEMA-PP 进行血小板粘附、细胞实验、大鼠皮下植入实验并与传统戊二醛交联猪心包膜作对比以表征 HEMA-PP 的抗血栓性、细胞相容性以及抗钙化性能。最后根据 ISO5840-3 的测试指导意见通过脉动流和加速疲劳试评估 HEMA-PP 的流体力学性能和耐久性以进一步验证 HEMA-PP 的临床应用潜力[2]。

结果与讨论:由于亲水层的引入,HEMA-PP 具有更好的抗血小板粘附性能。此外,亲水层能够保护细胞免受残余醛基的影响,HEMA-PP 具有更好的细胞相容性。在大鼠皮下植入后,HEMA-PP 周围聚集的免疫细胞更少,显示出更轻微的炎症反应。我们课题组之前的研究已经解释了细胞毒性可能导致生物人工心脏瓣膜钙化[3,4],因此具有更低细胞毒性的 HEMA-PP 表现出更低的钙化程度。HEMA-PP 已完成 4 亿次循环且在整个加速疲劳实验过程中保持适合的流体力学性能,结构完整、功能正常,满足 ISO5840-3 对生物瓣膜的流体力学性能和耐久性的要求。

结论:基于戊二醛的共交联以及后修饰策略改性的猪心包膜具有更好的细胞相容性、抗血栓性能、抗钙化性能,同时流体力学性能与耐久性均符合 ISO5840-3 对生物瓣膜的要求。这种基于戊二醛的共交联以及后修饰策略具有一定的应用潜力。

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FC03-P03

Caffeic acid cross-linked and post-modification for biological valve leaflet

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Background and purpose: The incidence of acquired valvular heart disease increases with age. Biological valves are now widely used in clinical practice, which were usually cross-linked by glutaraldehyde. However, with poor cytocompatibility and long-term calcification, glutaraldehyde cross-linked bioprosthetic valves have short service life. Therefore, it is of great significance to develop new cross-linking agents to replace glutaraldehyde. The stability, cytotoxicity, mechanical properties, and calcification of the bioprosthetic valves cross-linked with caffeic acid were investigated.

Methods: CA-PP was prepared by soaking fresh porcine pericardium (PP) in 5% caffeic acid ethanol solution activated by DMTMM for 24 h, followed by oxidation with ammonium persulfate for 12 h. CA-PP was subjected to collagenase degradation, cell compatibility, mechanical test and subcutaneous implantation in rats. The results were compared with glutaraldehyde cross-linked PP(GA-PP).

Results and conclusions: The absence of residual aldehyde groups and free glutaraldehyde in the CA-PP cross-link makes it less cytotoxic and conducive to endothelial cell proliferation. Immunochemical analysis of the implant material revealed fewer immune cells around CA-PP and a lower early inflammatory response. In addition, ICP-AES andAlizarin Red staining were used for quantitative and qualitative evaluation of calcification. The degree of calcification of CA-PP was much lower than that of GA-PP after 60 days of subcutaneous implantation in rats. The mechanical properties of CA-PP were comparable to those of GA-PP. Conclusion: CA cross-linking method is a novel non-glutaraldehyde cross-linking method with potential application.

FC03-P04

Anticoagulant and pro-endothelial functionalization modification for glutaraldehyde crosslinked bioprosthetic valves

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At present, the global prevalence of heart valve disease (HVD) is rising with the increase of age. Prosthetic heart valve replacement is an effective treatment for the HVD. In order to avoid thoracotomy and lifelong anticoagulant drugs, more and more patients are willing to choose bioprosthetic heart valves (BHVs) instead of mechanical heart valves (MHVs). All BHVs in clinical practice are crosslinked with glutaraldehyde (GA), but they still have drawbacks that lead to decay. As a xenogeneic implant material, BHVs have problems such as thrombosis, poor cytocompatibility, inflammation, and calcification. In this study, we constructed a polymeric hydrogel based on glycosaminoglycan and zwitterion, and applied it to the anticoagulant and proendothelial functionalization modification of glutaraldehyde crosslinked bioprosthetic valves while loading pro-endothelialization molecules. This functionalized modified glutaraldehyde crosslinked bioprosthetic valves (A-H-S-P) exhibited satisfactory stability and mechanical properties. Owing to the introduction of glycosaminoglycan and zwitterion, the hydrophilicity and antithrombotic properties of A-H-S-P were greatly improved. A-H-S-P had excellent cytocompatibility, and the dynamically released pro-endothelialization molecules can promote the growth and adhesion of human umbilical vein endothelial cells (HUVECs). In addition,

the results of rat's subcutaneous implantation showed that the inflammatory response and calcification of A-H-S-P were significantly reduced. In summary, this functionalization modification method based on glutaraldehyde crosslinked has greatly improved the anti-thrombotic, endothelialization, anti-inflammatory and anti-calcification properties of BHVs, extended the service life of BHVs, and has great application potential.

FC03-P05

静电喷涂席夫碱涂层改善 ZE21B 镁合金表面耐腐蚀性能

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心血管疾病是全世界过早死亡的主要原因,它不仅给人类带来巨大的痛苦,也给许多国家带来巨大的经济损失。目前,全世界每年有超过千万人死于心血管疾病(CVD)及其并发症,其中,动脉粥样硬化以及动脉狭窄是心血管疾病最主要致病因素。支架介入术是目前治疗心血管疾病的有效手段,其中生物医用镁合金以其优异的力学性能和可降解特性被认为是新一代心血管支架的优选金属材料,但其耐腐蚀性较差是其临床应用的主要限制因素。生物医用镁合金在体内环境中有很强的局部腐蚀倾向,这将严重影响其力学性能,不能充分发挥其预期的生物功能。缓蚀剂的应用是防止和减少金属材料腐蚀的一种常见而有效的方法。因此,使用缓蚀剂对镁合金表面进行修饰是提高其耐蚀性的有效途径。席夫碱是一种高效、无毒、易制备、易储存、成本低等优点的有机缓蚀剂。其分子结构中含有官能团(C=N-),能与 Mg²+、Zn²+等金属离子结合形成稳定的配合物,在金属材料防腐领域具有很大的潜力。本研究以丹皮酚和氨基酸为原料,通过静电喷涂法在 Mg-Zn-Y-Nd 合金(ZE21B 合金)表面制备了3种新的席夫碱复合席夫碱涂层,并以 ZE21B 合金为对照制备了3种单一席夫碱涂层。SEM和 XPS结果证实了该涂层的制备成功。浸泡试验和电化学试验表明,单一涂层和复合涂层均显著提高了 ZE21B 合金的耐蚀性,复合涂层可发挥协同缓蚀作用,表现出最佳的耐蚀性。本研究感谢国家自然科学基金(U2004164)的资助。

FC03-P06

脑血管用生物镁合金藤壶胶涂层的制备与评价

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缺血性卒中在世界范围内呈上升趋势,支架置入术已逐渐成为缺血性脑卒中的有效治疗方法之一。镁及镁合金材料因优异的机械性能和生物安全性,在心血管植入领域引起广泛关注。可生物降解镁合金 ZE21B 具有良好的力学性能和生物相容性,因此在血管支架中具有良好的应用前景。然而,降解过快和内皮化延迟是制约其进一步应用的瓶颈问题。藤壶分布于各类硬软质界面上,因其突出的界面粘附力而备受关注。目前已有研究发现,藤壶胶蛋白可以调节巨噬细胞表型 M2 表型,从而改善巨噬细胞的抗炎效果。Cp19k 在藤壶强底物结合中起关键作用。它的凝固和粘附机制是通过非共价相互作用来实现的,依靠具有-NH。和-OH侧链的氨基酸来去除界面处的水化层。已有研究表明-NH。可以取代吸附在表面的阳离子,从而增强附着力。本研究通过静电喷涂在 ZE21B 表面构建藤壶胶蛋白 cp19k 涂层,提高其耐腐蚀能力和促内皮化能力。将藤壶在各种基质上的粘附结构通过仿生学应用于脑血管支架,能够提高涂层与支架之间的结合力,减少血流剪切应力的影响,提高生物相容性。此后,通过电化学、静态浸泡腐蚀实验对涂层进行耐蚀性评价。实验数据表明 CP19k 能够有效提高底物 ZE21B 的耐腐蚀性,降低降解率。通过体外血液实验和细胞实验对涂层进行生物相容性评价,数据表明藤壶胶蛋白 cp19k 涂层抑制巨噬细胞粘附,调节巨噬细胞 M2 表型,降低炎症因子 TNF-α 的表达,抑制体内纤维增生,从而能够提高内皮细胞增殖和迁移能力,抑制平滑肌细胞增殖和调节收缩表型。研究数据表明,藤壶胶蛋白 cp19k 涂层在镁合金脑血管支架的表面改性上具有潜在的应用前景。本研究所用的藤壶胶蛋白来自 cp19k 国防科技大学胡碧茹教授的资助。

FC03-P07

镁合金血管支架表面 MOF/S-HA 复合涂层的构建及评价

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摘要:人类疾病死亡的原因之一是动脉粥样硬化,其已接近第一位,主要受影响部位有主动脉、冠状动脉、颈动脉和脑动脉,因此心肌梗塞和脑梗塞已成为这些血管疾病的主要后果。血管疾病的治疗已成为当务之急,血管内支架置入是目前最有效的治疗方法,但也存在一些亟待解决的问题,如不可降解金属支架异物残留、可降解金属支架降解速率不可控、内皮化不足、以及血脑屏障重塑困难等。近年来,金属有机骨架材料(MOFs)、透明质酸(HA)、肝素等功能分子在心脑血管植入材料表面改性领域得到广泛研究。镁(Mg)合金可降解支架在血管疾病的治疗中脱颖而出,镁几乎影响生命体的每一个功能,它是人体内第四丰富的元素,镁离子也是仅次于钾离子的第二大细胞间离子。镁在所有活细胞中发挥着重要作用,它是许多酶的辅助因子,而且它对人体神经系统起到保护作用。然而,用作植入材料的镁合金支架存在细胞相容性差、内皮化不足、血脑屏障重塑等困难。本研究将有机配体邻苯二酚(HPT)与 Cu(II)螯合后形成的 MOF-Cu 通过磺化透明质酸(S-HA)涂覆在 ZE21B 镁合金表面形成复合涂层,该涂层不仅继承了 S-HA 在具有优异的抗凝、抗炎特性的同时,还通过合理调节一氧化氮(NO)催化释放的浓度,显著提高涂层的生物相容性,促进内皮细胞的增殖、迁移和特定因子的表达(ECs),调节平滑肌细胞(SMCs)向收缩表型的转化,在促进巨噬细胞(MA)向抗炎 M2 表型转化方面具有重要而显著的表现。这些结果为镁合金血管支架材料重塑血脑屏障、舒张脑血管、抑制炎症反应、维持心脑血管弹性提供了重要的研究策略。

FC03-P08

一种增强血管支架用镁合金耐腐蚀性和生物相容性的复合席夫碱涂层

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引言: 镁合金的降解过快和内皮化延迟是限制其作为心血管支架材料的关键问题[1]。在探索新方法的过程中,缓蚀剂因其有效的防腐蚀和减蚀作用应用于镁合金专用涂层的设计中具有显著优势[2]。在前期的研究中,团队将丹皮酚分别与赖氨酸、甘氨酸、蛋氨酸进行脱水缩合反应合成了三种席夫碱缓蚀剂,并采用静电喷涂在 ZE21B 镁合金表面制备出复合席夫碱涂层。研究发现,复合席夫碱涂层比单一席夫碱涂层具有更显著的耐腐蚀能力[3]。

材料与方法:采用静电喷涂在 ZE21B 镁合金表面制备复合席夫碱涂层,制备方法参考文献[3],其中喷涂时间分别为 1min、1.5min、2min 和 2.5min,分别标记为 CP-1、CP-1.5、CP-2、CP-2.5。并对样品进行材料学表征、耐腐蚀性以及生物相容性测试。

结果与讨论:样品的表面形貌、粗糙度以及润湿性测试结果显示,CP-1.5 具有更均匀的表面和优异的亲水性。电化学测试结果显示,席夫碱涂层的自腐蚀电位得到提高,腐蚀电流密度明显减小,阻抗弧半径增大且具有较高的低频阻抗模量。此外,席夫碱改性后的样品也具有较高的极化电阻。电化学测试结果显示复合席夫碱涂层能够提高 ZE21B 合金的耐腐蚀性,且 CP-1.5 具有显著的缓蚀能力,与浸泡失重实验得出的结论一致。研究发现,涂层的缓蚀性能随着喷涂时间的变化表现出明显的浓度极值现象。内皮细胞的粘附与增殖结果显示,内皮细胞体外培养 72h 后,席夫碱涂层组的内皮细胞数目、铺展面积和长径比都得到了提高,其中 CP-1.5 发挥的作用优于其它席夫碱涂层,具有显著的促内皮化功能。血液实验结果显示,进行席夫碱喷涂的样品表面的血小板数目、纤维蛋白原的粘附与变性以及溶血率都低于裸 ZE21B 合金。其中 CP-1.5 表面呈现出较少的血小板粘附数目、较低的血小板激活水平和纤维蛋白原的粘附与变性水水平以及具有理想的溶血率,其具备较好的血液相容性。

结论: 复合席夫碱涂层均能不同程度的提升镁合金的耐蚀性和生物相容性。 当涂层喷涂时间为 1.5min

时,样品具有最佳的缓蚀性能以及更强的促内皮细胞粘附与增殖的能力,并具有较好的血液相容性。本研究可为生物降解镁合金血管支架专用涂层的设计提供参考。

FC03-P09

Near-Infrared Remotely Controllable Shape Memory Biodegradable Occluder Based on Poly(L-lactide-co-ε-caprolactone)/Gold Nanorods Composite

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Biodegradable occluders, which can efficiently eliminate the complications caused by permanent foreign implants, are considered to be the next-generation device for the interventional treatment of congenital heart disease. However, the controllability of the deployment process of degradable occluders remains a challenge. In this work, a near-infrared (NIR) remotely controllable biodegradable occluder is explored by integrating poly(L-lactide-co-\varepsilon-caprolactone) (PLCL) with polyethylene glycol modified gold nanorods (GNR/PEG). The caprolactone structural units can effectively increase the toughness of poly(L-lactide) and reduce the shape-memory transition temperature of the occluder to a more tissue-friendly temperature. Gold nanorods endow the PLCL-GNR/PEG composite with excellent photothermal effect. The obtained occluder can be easily loaded into a catheter for transport and spatiotemporally expanded under irradiation with near-infrared light to block the defect site. Both in vitro and in vivo biological experiments showed that PLCL-GNR/PEG composites have good biocompatibility, and the PEGylated gold nanorods could improve the hemocompatibility of the composites to a certain extent by enhancing their hydrophilicity. As a thermoplastic shape-memory polymer, PLCL-GNR/PEG can be easily processed into various forms and structures for different patients and lesions. Therefore, PLCL-GNR/PEG has the potential to be considered as a competitive biodegradable material not only for occluders but also for other biodegradable implants.

FC03-P10

Dressing Blood-Contacting Materials by a Stable Hydrogel Coating with Embedded Antimicrobial Peptides for Robust Antibacterial and Antithrombus Properties

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Although dressing blood-contacting devices with robust and synergistic antibacterial and antithrombus properties has been explored for several decades, it still remains a great challenge 1-2. In order to endow materials with remarkable antibacterial and antithrombus abilities, a stable and antifouling hydrogel coating was developed via surface-initiated polymerization of sulfobetaine methacrylate and acrylic acid on a polymeric substrate followed by embedding of antimicrobial peptides (AMPs), including WR (sequence: WRWRWR-NH2) or Bac2A (sequence: RLARIVVIRVAR-NH2) AMPs. The chemical composition of the AMP-embedded hydrogel coating was determined through XPS, zeta potential, and SEM-EDS measurements. The AMP-embedded antifouling hydrogel coating showed not only good hemocompatibility but also excellent bactericidal and antiadhesion properties against Gram-positive and Gram-negative bacteria. Moreover, the hydrogel coating could protect the AMPs with long-term bioactivity and cover the positive charge of the dotted distributed AMPs, which in turn well retained the hemocompatibility and antifouling capacity of the bulk hydrogels. Furthermore, the microbiological results of animal experiments also verified the anti-infection performance in vivo. Histological and immunological data further indicated that the hydrogel coating had an excellent anti-inflammatory function. Therefore, the

present study might provide a promising approach to prevent bacterial infections and thrombosis in clinical applications of blood-contacting devices and related implants.

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FC03-P11

A Versatile Glycopeptide Hydrogel Promotes Chronic Refractory Wound Healing Through Bacterial Elimination, Sustained Oxygenation, Immunoregulation, and Neovascularization

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Chronic refractory wounds have become a severe threat to public health and are characterized by repeated bacterial infections, persistent hypoxia, abnormal immune regulation, and obstruction of angiogenesis. However, current treatment strategies usually perform only one or two therapeutic functions and cannot satisfy the dynamic and complex demands of chronic wound healing. Herein, a versatile dynamic Schiff base and borate ester crosslinked glycopeptide hydrogel was prepared from phenylboronic acid-grafted \varepsilon-polylysine (EPBA), epigallocatechin-3-gallate (EGCG), and oxidized alginate. Customized polydopamine-coated honeycomb MnO2 nanoparticles loaded with herb-derived salvianolic acid B (PHMS) were embedded into the hydrogel before gelation. Under the distinct acidic and oxidative microenvironment of chronic refractory wounds, the hydrogel gradually dissociates, and the released EPBA effectively eliminates bacteria, while the released EGCG and PHMS eradicates reactive oxygen and nitrogen species, promotes M2 polarization of macrophages, and continuously generates oxygen. Then PHMS further disintegrates, and the released salvianolic acid B promotes angiogenesis through the PI3K/Akt pathway. The versatile glycopeptide hydrogel accelerates Staphylococcus aureus-infected diabetic cutaneous wound repair in vivo and is a promising candidate dressing for chronic refractory wound healing.

FC03-P12

Application of Bioactive Functional Materials in Osteomyelitis

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Orthopedic doctors are puzzled by osteomyelitis because the rate of incidence is high, treatment costs are high, and the disease easily recurs after treatment. The conventional treatment for osteomyelitis includes surgical debridement combined with long-term local or systemic high-dose antibiotics. However, the clinical efficacy of osteomyelitis treatments remains unsatisfactory and may cause severe bacterial resistance. At present, the combination of biomaterials for the treatment of osteomyelitis is a hot topic in biomedical research and exhibits significant advantages, which help overcome the clinical challenges of osteomyelitis treatment. Biomaterial carriers, such as bone cement, hydroxyapatite, hydrogels, and nanoparticles, can be used to deliver therapeutic active substances directly to the diseased site to reduce side effects, increase efficacy, and reduce bacterial resistance. This review provides an overview of the biological manifestations and latest research progress of

biomaterials in the treatment of osteomyelitis, explores design ideas and mechanisms of action of these biomaterials, and presents prospects for their medical research and clinical applications. It is hoped that this review will inspire the development and clinical transformation of biomaterials for the treatment of osteomyelitis.

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A Novel Smart Hydrogel Dressing, Containing Antimicrobial Peptides and Quercetin, Enhances the Healing of Chronic Infectious Diabetic Wounds through Dual-Barrier Drug Delivery Action

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Chronic diabetic wounds struggle to heal due to drug-resistant bacterial infections, oxidative stress microenvironment, and immune dysfunction. At present, the disease has become a huge clinical challenge. Currently, hydrogel dressings designed for diabetic wound healing typically offer one or two therapeutic functions, making it challenging to address the wound's complex pathological environment and achieve effective treatment. In this research, a hydrogel dressing with bactericidal and anti-inflammatory properties was synthesized by crafting a pH/ROS responsive scaffold from phenylboronic acid-grafted hyaluronic acid (HA-PBA) and 4-arm-PEG-dopamine (4A-PEG-Dopa), employing dynamic borate ester bonds. This structure was then infused with the antimicrobial peptide (AMP) and ROS-sensitive micelle mPEG-TK-PLGA loaded with quercetin (QC). This dressing embodies a dual-barrier drug delivery mechanism, engineered for the prolonged and consistent liberation of QC. In the experiment, the hydrogel dissociated within the acidic microenvironment of diabetic wounds, thereby liberating the encapsulated micelles and AMP. Upon further dissociation, the micelles release QC due to ROS-abundant micro-environment, which could relieve oxidative stress and encourages M2 polarization of macrophage via the Akt/STAT6 signaling pathway. Therefore, this smart delivery system, developed through our innovative approach, holds promise for treating chronic infectious diabetic wounds.

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表面引发构筑 ROS 吸收海绵涂层及其抗血栓应用研究

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Thrombosis of cardiovascular implantable devices is life-threatening, with an increased risk of vascular complications such as infection, pulmonary embolism, or vascular damage after implantation. The antithrombotic drugs not only can not completely prevent thrombosis and even the risk of bleeding. Thrombosis is an innate immune process involving a variety of molecular mechanisms. By regulating the immune response and improving the local microenvironment to prevent thrombus formation in implanted devices may be another strategy. Herein, we prepared a selenium-containing hydrogel sponge coating on polyurethane catheters, which was formed by redox-initiated monomer polymerization at the substrate interface, like a hydrogel growing from the inside of the substrate, which was a stable and long-lasting coating. Sodium selenite seeds were seeded in the hydrogel precursor solution and reduced in situ to form nano-selenium particles in the hydrogel, which could continuously absorb local excess reactive oxygen species through the powerful antioxidant and anti-inflammatory effects of nano-selenium. The super-lubricity of the hydrogel coating imparted strong resistance proteins and cell adhesion ability to the coated device, and our results revealed that the selenium-containing hydrogel coating can significantly reduce proinflammatory cytokines secretion and promote the anti-inflammatory phenotypic transition of macrophages. Furthermore, we tested that the hydrogel-coated intravenous catheter was effective in inhibiting

vascular lesions and thrombosis compared with bare catheters after implantation in the rabbit jugular vein. The study designed a stable and long-lasting hydrogel sponge coating to continuously exert antioxidant effect and prevent thrombosis by improving the local immune microenvironment, which provides a new idea for the application of implantable devices.

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生物人工心脏瓣膜非戊二醛交联化及表面修饰研究

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With an aging population, the patients with valvular heart disease (VHD) are growing worldwide, and valve replacement is a primary choice for these patients with severe valvular disease. Among them, bioprosthetic heart valves (BHVs), especially BHVs trough transcatheter aortic valve replacement, are widely accepted by patients on account of their good hemodynamics and biocompatibility. Commercial BHVs in clinic are prepared by glutaraldehyde cross-linked pericardial tissue with the risk of calcification and thrombotic complications. In the present study, a strategy combines improved hemocompatibility and anti-calcification properties for BHVs has been developed based on a novel non-glutaraldehyde BHV crosslinker hexakis(hydroxymethyl)melamine (HMM) and the anticoagulant fucoidan. Besides the similar mechanical properties and enhanced component stability compared to glutaraldehyde crosslinked PP (G-PP), the fucoidan modified HMM-crosslinked PPs (HMM-Fu-PPs) also exhibit significantly enhanced anticoagulation performance with a 72 % decrease in thrombus weight compared with G-PP in ex-vivo shunt assay, along with the superior biocompatibility, satisfactory anti-calcification properties confirmed by subcutaneous implantation. Owing to good comprehensive performance of these HMM-Fu-PPs, this simple and feasible strategy may offer a great potential for BHV fabrication in the future, and open a new avenue to explore more *N*-hydroxymethyl compound based crosslinker with excellent performance in the field of biomaterials.