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Editorial: Responsive Biomaterials for Tissue Regeneration

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Editorial on the Research Topic

Responsive Biomaterials for Tissue Regeneration

Biomaterials for tissue regeneration have been evolving rapidly within the past several decades, bringing numerous exciting promises in enhancing the innate healing/regeneration capabilities and/or treating the defects, losses, or dysfunctions of human body tissues/organs. However, tissue regeneration processes are usually complicated, requiring to orderly regulating the behaviors and functions of different cell types by dynamic cell microenvironments in a specific spatiotemporal manner. It would be extremely difficult to be perfectly fulfilled by biomaterials with only static features or properties. To address this challenge, responsive biomaterials with dynamic characteristics have been recently emerging, aiming to mimic the native cell microenvironments and subsequently better promoting tissue regeneration. On basis of extensive innovations of stimuli-responsive materials such as shape memory polymers, functional hydrogels, and photochromic molecules, increasing responsive biomaterials have been developed and offered unprecedented possibilities in manipulating cell behaviors and functions on demand. Nevertheless, various challenges and problems remains so far in the field that significantly affect the perspectives of translational applications of responsive biomaterials, including but not limited to the design and developments of new materials for better meeting the requirements in a specific occasion and the biocompatibility and bioactivity of the materials. To summarize recent advances in this field, as well as to provide a platform for exchanging opinions and sharing findings on tracking the challenges of the field, we organized this Research Topic of *Frontiers in Materials* and *Frontiers in Bioengineering and Biotechnology*, which focuses on "Responsive biomaterials for tissue regeneration." The Research Topic include three research articles, covering different topics ranging from the design and fabrication of new responsive biomaterials to systematical biological evaluations of novel biomaterials in practical occasions.

Drug-eluting biomaterials have been widely investigated for various biomedical applications. On-demand control over the release profiles of the therapeutic agents is the major goal in the field. To enhance the controllability of the molecular release for the drug-eluting biomaterials, Lin et al. designed and fabricated photo-responsive hydrogels based on a photochromic molecule, azobenzene (AZO), and investigated the employments of such hydrogels in preparing functional drug-eluting contact lenses with light-controlled release profiles of model drugs (article number 680359). In this study, the researchers synthesized two kinds of cross-linkable AZO molecules as monomers and crosslinkers, subsequently preparing functional AZO copolymerized and AZO crosslinked hydrogels. Orfloxacin and puerarin, small molecular drugs commonly used in the treatment of ophthalmic diseases, were used as model drugs to be incorporated within the hydrogel, resulting in functional drug-eluting contact lenses. Owing to the photoisomerization of the AZO molecules, the

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resultant functional AZO copolymerized and AZO crosslinked hydrogels both exhibited photo-responsive swelling behaviors. The photo-controllable reversible and stable swelling behaviors of the consisting hydrogels made the release profiles of the incorporated model drugs tunable accordingly from the functional drug-eluting contact lenses. The functional drug-eluting contact lenses with photo-responsive controlled drug release behaviors hold great promise in ophthalmic healthcare and treatment.

Biocompatibility and bioactivity are always predominant concerns for novel biomaterials to be used in human body. For evaluating the biocompatibility and bioactivity of a type of frequently used biomaterials in dental, pulp-capping agent, Kuo et al. established detailed methodologies and conducted systematical *ex vivo* and *in vivo* assessments for different forms of pulp-capping agents, including an experimental agent, white-colored mineral trioxide aggregate (WMTA), and commercial agents, iRoot BP Plus and Biodentine (article number 738430). Using *ex-vivo* human tooth culture model and *in vivo* miniature pig model, they compared the color stability of the cements and pulp responses among different groups. The results proved superior properties of the experimental one in the performances of discoloration and assisting the formation of mineralized foci. Through *in vivo* assessments using miniature pig model, it was also demonstrated that the novel WMTA induced the formation of thickest dentin bridge with normal tubular anatomical structures, revealing decent biological properties of the novel dental biomaterials. To address the challenges of synthetic biomaterials such as foreign body responses and mechanical mismatches, Lu et al. exploited natural swine and bovine pulmonary visceral pleura (PVP) as novel biomaterials and evaluated their biocompatibility and biological performances for artery patch-angioplasty in detail (article number 679466). Using a swine model of high-fat diet, the researchers implanted the cross-linked PVP as patches in the carotid artery and evaluated the patency and tissue neo-formation in the surgical sites through medical imaging and histological analyses. The results showed that the PVP patches exhibited excellent biocompatibility and bioactivity. All the arteries at 4 months postoperative remained patent with no complications even though for the pigs with high thrombogenesis risks. The PVP patches also demonstrated desirable bioactivities in promoting the neo-formation of different vascular tissue layers identical to the normal anatomies of native arteries, as well as implying the signs of restoration of vascular functions for animals with hypercholesterolemia. The results of systematical *ex vivo* and particular *in vivo* investigations would pave avenues for the further translational applications of novel biomaterials in clinic.

Responsive materials for tissue regeneration are emerging research areas relevant to a broad range of subjects such as material science, chemistry, biology, biomedical engineering, and medicine. The advances of the field will certainly need the involvements of more and more researchers and multi-disciplinary efforts. As Guest Editors of *Frontiers in Materials* and *Frontiers in Bioengineering and Biotechnology* for the Research Topic of "Responsive biomaterials for tissue regeneration," we would like to acknowledge deeply the contributions of all the authors and reviewers. We hope that the papers included in this research topic could attract broad attention of researchers from different disciplines and look forward to envisioning the rapid progress of the emerging field with inter-disciplinary cooperation.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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