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Letters to Editor

Engineering cellular metabolism for regenerative medicine: The role of bioenergetic materials

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In recent years, the role of cellular energy homeostasis as a key regulator in tissue regeneration has garnered increasing attention within the regenerative medicine community. Traditionally, biomaterials have been designed primarily to provide structural support and biochemical signals. However, emerging evidence suggests that the regulation of cellular metabolism, particularly mitochondrial function, redox homeostasis, and bioenergetic signaling is a critical determinant of successful tissue repair and regeneration [1,2]. In this context, we aim to emphasize the evolving concept of bioenergetic materials, a class of engineered biomaterials specifically designed to modulate cellular metabolic pathways and improve regenerative outcomes.

Recent studies have elucidated how metabolic reprogramming can influence stem cell fate, immune responses, and overall tissue healing. Notably, interventions targeting mitochondrial dynamics, Adenosine triphosphate (ATP) synthesis, and reactive oxygen species (ROS) balance have demonstrated considerable potential in promoting tissue regeneration in various preclinical models. For example, biomaterials capable of delivering key metabolic cofactors including Nicotinamide adenine dinucleotide (NAD^+), Flavin adenine dinucleotide (FAD), and mitochondrial-targeted antioxidants have been shown to enhance cell survival under hypoxic or inflammatory conditions and accelerate repair in ischemic, degenerative, and traumatic tissue injuries [3,4].

A particularly compelling example involves the use of cerium oxide nanoparticles (CeO_2 NPs). These nanoparticles leverage their unique redox properties, mediated by reversible Ce^{3+}/Ce^{4+} transitions, to stabilize mitochondrial membrane potential, reduce oxidative stress, and support ATP production. Incorporating CeO_2 NPs into bioactive scaffolds such as electrospun membranes or mesoporous frameworks has been reported to significantly enhance stem cell proliferation, osteogenic differentiation, and even neuronal tissue repair. Moreover, the development of hybrid systems such as Ce-based metal-organic frameworks (MOFs) functionalized with biological molecules like keratin demonstrates how bioenergetic modulation can be synergistically combined with immunomodulatory and mechanical functions to optimize regenerative efficacy [5-7].

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Beyond cerium-based constructs, mitochondria-targeted delivery platforms including Coenzyme Q10 (CoQ10)-loaded liposomes, MitoQ-based nanoparticles, and NAD^+-enriched systems have shown promising outcomes in various regenerative models, such as myocardial infarction, chronic wounds, and neurodegenerative diseases. These systems restore mitochondrial function, mitigate oxidative damage, and promote anabolic cellular processes essential for tissue recovery. Similarly, ROS-scavenging scaffolds and bioenergetic hydrogel matrices are being actively explored for their capacity to rescue dysfunctional mitochondria and foster an environment conducive to regeneration [8-10].

Despite the significant promise of bioenergetic materials, critical challenges remain. Comprehensive long-term *in vivo* studies are necessary to elucidate the systemic and off-target effects of chronic metabolic modulation. Furthermore, the lack of standardized assays for evaluating bioenergetic performance across different materials hampers reproducibility and regulatory progress. There is also an unmet need to explore how bioenergetic materials can be integrated with bioelectrical stimulation, gene delivery systems, and immunomodulatory platforms to create multifunctional regenerative interfaces.

In conclusion, the paradigm of bioenergetic materials marks a transformative shift in regenerative medicine, moving beyond passive scaffolding toward metabolically active platforms capable of orchestrating cellular energy dynamics. We strongly advocate for intensified interdisciplinary collaboration to optimize, validate, and translate these materials from bench to bedside. Advancing this frontier holds the potential to unlock next-generation regenerative therapies with unprecedented precision and efficacy.

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Authors' contributions

AH, AA: Conceptualization, Project administration, Supervision, and editing. AH, SSA, AA: Data collection, Writing original draft, and editing. All authors read and approved the final version of manuscript.

Conflict of interest

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