

## Biofunctional Biomaterials – The Next Frontier

**T**raditional medical devices only partially replicate the structural and biophysical properties of the tissues to be replaced. Clinical data indicate that these systems fail to recapitulate native tissue function, necessitating the development of new biofunctional tissue equivalents. The driving hypothesis of this research is that these biofunctional biomaterials will positively interact with the host and through their biophysical, biochemical, and/or biological cargo will stimulate the innate reparative machinery, thereby promoting functional repair and regeneration. Thus, biofunctional biomaterials are at the forefront of scientific and technological research and innovation.

Among others, tissue-specific geometrical conformation (e.g., channels, fibers) and dimensionality (e.g., nano, micro) determine cell fate through cytoskeleton activated transduction pathways. This spatially dependent cellular control has aspired development of biofunctional devices with a high level of tissue-specific architectural biomimicry. Indeed, advancements in engineering have made available numerous nano- to micro-fabrication technologies that have enabled the development of two- and three-dimensional implantable devices with precise spatial organization down to the nanometer level. Such biofunctional biomaterials offer control over cell motility, maintain permanently differentiated cell phenotype, direct stem cell lineage commitment, and facilitate directional neotissue development.

Aging, injuries, and pathophysiologies are often associated with decreased biological activity of host cells and insufficient reparative host mechanisms. To this end, bioengineering and bioconjugate (bio)chemistry have joined forces to provide tools for sustained and localized delivery of various payloads, including drugs, biologics, and viable cell populations, that will enable functional repair and regeneration. Outputs of this transdisciplinary collaboration include numerous biomaterial-based carriers (e.g., particles, spheres), chemical systems (e.g., dendrimers, stimuli responsive polymers), and biological molecules (e.g., peptides) that aim to boost reparative cascades.

Collectively, biophysical, biochemical, and biological functionalization strategies are and will play a pivotal role in reparative therapies associated with current unmet clinical indications, such as injuries and pathophysiologies of human body systems, immunodeficiency disorders, and autoimmune diseases. Thus, biofunctional biomaterials will be a core element of future bedside therapies, significantly contributing in improving human health and well-being and notably reducing healthcare expenditure.

In this special issue, review papers describe the evolution of biofunctional biomaterials and advancements achieved in recent years, while original research papers provide a snapshot of emerging technologies and next frontiers in the field of biofunctional biomaterials for biomedical applications. It is clear that advancements in (bio)engineering, (bio)chemistry, and biology have significantly expanded our toolbox toward functional repair and regeneration. In the years to come, regulatory compliance and efficacy studies in preclinical and

clinical settings will bring the newly developed knowledge to the technology readiness level suitable for clinical translation and commercialization.

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#### Notes

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