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Advanced nanobiomaterials for tissue engineering and regenerative medicine

"...this special issue of Nanomedicine will provide readers with information on the application of nanobiomaterials and nanotechnologies in the field of tissue engineering, from aspects of design considerations for fundamental manipulation of cell-material interaction to material synthesis and full fabrication of tissues."

The ultimate goal of tissue engineering and regenerative medicine is to develop functional substitutes to restore, repair or replace damaged tissue and/or organs. In tissue engineering, as well as improvising the direct constituents, such as scaffolds and cells, the supporting technologies for monitoring, characterizing and evaluating the development of the engineered tissue are equally crucial.

Nanotechnologies clearly have had an impact on tissue engineering, in both a direct and indirect manner. First, the natural niche of cells, the extracellular matrix, is structurally hierarchical and nanocomposite in nature. Understanding this niche and taking the biomimicking route has proven to bring tremendous improvement to the field of tissue engineering. This progress follows closely behind the advancement of enabling tools, especially in the micro- and nano-fields where only within these fields could cells be effectively probed, monitored, characterized and understood.

Therefore, this special issue of *Nanomedicine* will provide readers with information on the application of nanobiomaterials and nanotechnologies in the field of tissue engineering, from aspects of design considerations for fundamental manipulation of cell-material interaction to material synthesis and full fabrication of tissues.

Contributors & their work

The contributors of this special issue are experts in their own areas and have very diverse expertise, which reflects the interdisciplinary nature of tissue engineering and nanotechnologies.

Chua is an expert in rapid prototyping and additive manufacturing in Singapore, as well as internationally. For the past 14 years, his research focus has been on utilizing and advancing additive manufacturing in different areas,

including 3D tissue engineering scaffold fabrication via additive manufacturing techniques such as selective laser sintering and computer-aided systems using parametric polyhedral. Chua and colleagues contribute a review article on nanobiomaterial strategies for the development of organized tissues and organ constructs [1]. The challenges and future prospects of applying these strategies, especially in bioprinting, are also outlined.

Tan's research focuses on biodegradable polymers, drug delivery, cell-material interaction, engineering the stem cell niche and tissue engineering in general. Tan and colleagues have presented an extensive review on using micro-/nano-surfaces to engineer cellular responses. In this special focus issue, they discuss the mechanotransduction events associated with these micro-/nano-structures and provide future perspectives of this niche engineering [2].

Wang's research focuses on biomaterials, tissue engineering and regenerative medicine with particular focus on bioresponsive biomaterials for therapeutic 3D scaffolding and cell delivery, gene/antisense delivery for regenerative medicine, stem cell application for tissue regeneration and tissue-biomaterial integration for *in situ* tissue engineering. The particular contribution of his review article is to conceptually elaborate both the denotation and connotation of bioresponsive hydrogel materials, and also to update the progress and prospects of their applications in tissue engineering and regenerative medicine [3].

Bartolo is a world renowned expert in the field of advanced manufacturing processes, including additive manufacturing and biomanufacturing. In this special issue, Bartolo and colleagues contribute a review on *in situ* bioprinting of skin constructs [4]. The review details how to combine biomaterials, cells, growth factors

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and advanced biomanufacturing techniques for the fabrication of constructs that mimic the skin anatomy and promote the regeneration of healthy and vascularized tissues.

Li's research interests and activities include synthesis of polymer nanoparticles for drug and gene delivery, controlled drug release using hydrogels, development of advanced nanocomposites, fabrication of micro- to nano-sized drug particles, and polymer rheology and processing, among others. Li and colleagues review the recent progress in studying and developing nanocomposites for bone tissue regeneration [5]. The article covers aspects of interest such as biomimetic synthesis of bone-like nanocomposites, guided bone regeneration from inert biomaterials to bioactive nanocomposites and nanocomposite scaffolds for bone regeneration. In addition, the design, fabrication, and *in vitro* and *in vivo* characterization of such nanocomposites are also reviewed.

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Nguyen's research group is focused on microfluidics, nanofluidics, micro-/nano-machining technologies, micro-/nano-scale science and development of instrumentation for biomedical applications. Recently, the group's work has focussed on multiphysics and multidisciplinary aspects of microfluidic technology resulting in emerging fields, such as micro-optofluidics and micro-magnetofluidics. For applications in biology and nanomedicine, Nguyen's group aims to develop *in situ* platforms that can mimic *in vivo* conditions. These platforms would provide a 3D environment, and chemical and mechanical stimuli for cell growth and drug testing. His research article in this special focus issue focuses on the development of a microdevice for well-controlled mechanical strain, an important mechanical stimulus for cell growth [6]. The platform is also designed for real-time imaging with microscopy, presenting a powerful tool for biomedical research.

Chian's areas of expertise are polymer chemistry, medical implants and tissue engineering. His current research focuses on the synthesis of degradable polymers, tissue engineering and scaffold fabrication technology. Following their previous works on 'cryogenic electrospinning',

here Chian and colleagues propose a mechanism to investigate the role of ice crystals in expanding the pores of cryogenic electrospun scaffolds [7]. A bilayered scaffold consisting of distinctly different pore sizes is also fabricated for coculture of dermal fibroblasts and keratinocytes.

Ng's research interests lie in the basic understanding of cell-material interactions within the scope of tissue engineering and biomaterial development, and his group aims to translate basic understanding into clinically relevant applications. He has specific expertise in the areas of soft tissue engineering, development of hair keratin as a biomaterial and nanotoxicology. His article describes the successful production of a fibrous matrix by electrospinning a concentrated solution of human hair keratins [8]. Chemical characterization of the matrix was performed along with demonstration of its cell compliance with fibroblasts. The results of this paper contribute another step in the development of human hair keratins as a biomaterial for biomedical applications. In particular, electrospun keratin matrices have the potential to be used as templates for soft tissue regeneration.

Fong's research interests are in synthetic biology, protein engineering and cell biology for both biological and engineering applications, design and synthesis of artificial protein biomaterials, developing assays for studying collective migration in 2D and 3D environments, engineering proteins with novel functions, and improving microbial systems for efficient synthesis of protein materials. Fong and colleagues present the development of novel elastin-like materials with antibacterial capabilities and demonstrate the potential of artificial protein materials for use as wound dressings and biomedical implant coatings [9].

Wang's research interests include biomedical materials (in various forms: single component or composite, dense or porous, bulk or coating, particulate or fibrous, single crystals), *in vitro* and *in vivo* evaluation of biomaterials, tissue engineering, materials and systems for controlled release of biomolecules/drugs, therapeutics, surface engineering and nanotechnology. In this special focus issue, Wang and co-authors report negative voltage electrospinning of fibrous nanocomposite scaffolds bearing negative electric charges (N-poled scaffolds) and discuss how retained negative charges could influence the biological performance of scaffolds for bone tissue engineering [10].

In addition to reviews and research articles, three editorials are also included in this special

focus issue to offer readers alternative thoughts and opinions on recent issues related to tissue engineering. Primo and Claudio propose that a combination of research in pharmaceutical technology, photodynamic processes and tissue engineering could improve current medical protocols to achieve a better and longer life [11]. Amler *et al.* comment on the current status and potential of coaxial nanofiber systems for cartilage applications [12]. Fisher and Mauck offer their opinions on the use of nanofibrous scaffolds for engineering orthopedic tissues [13]. While presenting the promising aspects and highlighting the current issues on 3D construct complexity and organization, they also raise and discuss future questions, such as ‘how much of the native structure do nanofibrous scaffolds

need to match in order to be effective?’ This special focus issue also features an interview with Webster [14], renowned expert in the field of nanostructured biomaterials and an overview of some of the most recent topical publications in the field, discussed by Sehgal and Banerjee [15].

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