



Propelling Biomaterial Innovations for Advanced Cell Therapy

At the heart of biomaterials research lies the pursuit of enhancing human well-being.

Translational regenerative medicine is a dynamic and rapidly advancing field that requires multi-disciplinary research approaches to develop innovative clinical solutions, therapies, and devices to improve human health and well-being. Dr Xin ZHAO, Limin Endowed Young Scholar in Biomaterials and Tissue Engineering, Associate Professor in Department of Applied Biology and Chemical Technology of The Hong Kong Polytechnic University (PolyU), is at the forefront of this field.



Dr Xin ZHAO

Limin Endowed Young Scholar in Biomaterials and Tissue Engineering

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Highly Cited Researcher:

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Dr ZHAO's research interests involve the integration of multidisciplinary approaches, combining various fields such as material science, cell biology, engineering and medicine. The focus of her studies is on modulating cell microenvironments, manipulating cell behaviours and advancing tissue-engineered organ development. To synthesise patient-oriented biomaterials with unique structures and properties, her research team actively investigates how cells sense, interact and develop with biomaterials to regenerate damaged or diseased tissues.

Dr ZHAO said, “I begin by conducting a comprehensive study of the needs and developing a fundamental understanding of the clinical problem. I then design biomaterials with tailored features and structures to provide effective solutions.”

Specifically, photocrosslinkable polymers play a pivotal role in the research. They have garnered significant attention in the field of regenerative medicine due to their mild polymerization conditions, highly tunable physical properties, excellent biocompatibility and precise spatiotemporal

control. These polymers offer immense potential for replacing or regenerating diseased or damaged tissues, such as skin and bone. In her research journey, Dr Zhao endeavours to develop and advance the revolutionary application potential of these materials for tissue engineering.

Uncovering practical uniqueness

Dr ZHAO's discovery of the Photocrosslinkable Gelatin (GelMA) hydrogel offers a breakthrough solution in epidermal tissue engineering, which exceeds the conventional limitations of collagen- or gelatin-based hydrogels. Due to its tunable mechanical, degradation, and biological properties, GelMA hydrogel emerges as a promising option for various applications, such as epidermal substitutes, wound dressings, or substrates, to construct various in vitro skin models.

The research “Photocrosslinkable Gelatin Hydrogel for Epidermal Tissue Engineering” was published in *Advanced Healthcare Materials*, and has garnered widespread citations.¹





The ability of cells to attach, spread and grow on hydrogels is fundamentally important to tissue development. Photocrosslinkable GelMA hydrogel with tunable mechanical and degradation features ideally makes it suited for skin-tissue engineering scaffolds. By varying the concentration of GelMA prepolymer solution, the physical and biological properties of the resulting hydrogels could be adequately controlled to meet the requirement for epidermis formation.

Hydrogels of higher concentrations display improved material mechanical and degradation properties for cell adhesion and keratinocyte monolayer formation. Also, GelMA hydrogels support the formation of a stratified epidermis with certain barrier functions such as electrical resistance and prevention of water loss.

Persistent pursuit of novel approaches

Dr ZHAO and her research team have showcased the exceptional processability of photocrosslinkable polymers, rendering them inherently compatible with a diverse range of biomanufacturing technologies. Their groundbreaking work has unveiled a multitude of new possibilities in this field.

Stem cell transplantation has emerged as a promising treatment for various injuries ranging from bone fractures to bone cancers and for other disorders. Very often, bone marrow-derived mesenchymal stem cells (BMSCs) are used for bone regeneration due to their osteogenic differentiation potential. In this research area, Dr ZHAO presents a strategy of microfluidics-assisted technology encapsulating BMSCs and growth factors in photocrosslinkable GelMA microspheres to ultimately generate injectable osteogenic tissues constructs.

The findings were published in *Advanced Functional Materials*, titled "Injectable Stem Cell-Laden Photocrosslinkable Microspheres Fabricated Using Microfluidics for Rapid Generation of Osteogenic Tissue Constructs". The research demonstrated that the GelMA microspheres can sustain stem cell viability and proliferation, support cell spreading inside the microspheres, and facilitate migration from the interior to the surface.²

In vitro and in vivo studies showed that BMSCs encapsulated GelMA microspheres exhibit enhanced osteogenesis. This approach holds promise for facilitating bone regeneration with minimum invasiveness and can potentially be combined with other matrices for broader applications.



Putting patients at the centre

"Scientific research is a highly dynamic field that demands continuous innovation. It allows us to delve into fascinating new phenomena and discover unexplored realms that undoubtedly broaden our horizons," said Dr ZHAO.

Large-scale bone defects caused by injuries, diseases, or trauma impose significant challenges in orthopaedic surgery due to the limited capacity of damaged bone tissues for self-repair and complete remodelling. Dr ZHAO has persistently investigated a new approach to advance therapeutic development in this area. In particular, for 3D printing, it shows great potential in the rapid and accurate fabrication of bone tissue engineering scaffolds to the patients' needs.

Dr ZHAO's team envisions the novel photocrosslinkable nanocomposite ink as an ideal candidate for 3D printing bone grafts. The research "Photocrosslinkable nanocomposite ink for printing strong, biodegradable and bioactive bone graft"

was published in *Biomaterials* and has received significant attention.³

Compared with commonly used polymer or composite inks, the proposed material holds great promise in the 3D printing of bone grafts tailored to meet the specific needs of patients. This is attributed to its suitable rheological characteristics, rapid photocrosslinking solidification, adequate mechanical strength and toughness, tunable degradation rate and excellent bioactivity. Both in vitro and in vivo studies demonstrated excellent biocompatibility and osteogenic potential of the printed nanocomposite scaffolds.

Dr ZHAO said, "I believe that accumulating numerous citations is a cherished goal for every researcher. By making a high impact with research, it inspires further exploration and expands the functionality and applications of the developed materials. These collective efforts foster the development of superior materials and innovative solutions to clinical challenges."

Research Interests

Biomaterials, Drug Delivery, Tissue Engineering, Cell Micro-environment, Microfluidics

Selected Publications

1. X. Zhao, Q. Lang, L. Yildirimer, Z. Lin, et.al., Photocrosslinkable Gelatin Hydrogel for Epidermal Tissue Engineering, *Advanced Healthcare Mater*, vol 5, Jan 2016
2. X. Zhao, S. Liu, L. Yildirimer, H. Zhao, et.al., Injectable Stem Cell-Laden Photocrosslinkable Microspheres Fabricated Using Microfluidics for Rapid Generation of Osteogenic Tissue Constructs, *Advanced Function Mater*, vol 26, May 2016
3. X. Zhao, Y. Yang, Q. Zhang, T. Xu, et.al., Photocrosslinkable nanocomposite ink for printing strong, biodegradable and bioactive bone graft, *Biomaterials*, vol 263, Dec 2020

