The Chinese University of Hong Kong
Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

Student : Mr. YUAN Weihao
Supervisor : Prof. BIAN Liming
Date : 18 May, 2021 (Tuesday)
Time : 10:00 am
Zoom Link : https://cuhk.zoom.us/j/3910170764?pwd=NmpxdFQvUFZZM2NlWFZ6RGJ5SWYwQT09
Meeting ID : 391 017 0764
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Title: Engineered Dynamic Biomaterials for Manipulation of Cell Behaviors and Tissue Regeneration

Cells continuously interact with their surrounding microenvironment, and these interactions regulate a series of cellular processes, thereby directing cell behaviors and fate. Engineered biomaterials provide an artificial microenvironment for the seeded or encapsulated cells, where cell–material interaction can be rationally modulated to realize effective cell lineage commitment. However, the field of dynamic synthetic biointerfaces, which can be utilized for manipulation of cell–material interaction, is still in its infancy. In this dissertation, we present three different dynamic platforms to emulate the inherent properties of ECM, manipulate the cell behaviors and fate, and promote the tissue regeneration.

Among various biomaterials, hydrogels are the promising candidates for tissue engineering and regenerative medicine. We next moved our focus to dynamic hydrogels based on metal ions and bisphosphonates. We first developed a versatile and general strategy to fabricate a family of nanocomposite hydrogels based on a wide array of metal ions. We demonstrated that the hydrogels exhibited a wide spectrum of remarkable dynamic properties, such as excellent injectability, rapid stress relaxation, efficient ion diffusion, and triggered disassembly for harvesting encapsulated cells. We next applied the developed hydrogels to treat peripheral nerve injuries, which are of great clinical significance. We demonstrated that the nanocomposite hydrogels containing magnesium and bisphosphonates promoted peripheral nerve regeneration and achieved partial functional recovery in s sciatic nerve injury rat model.

To further investigate the applications of tissue regeneration assisted by the dynamic hydrogels, we next designed a supramolecular cell-adaptable gelatin host-guest (GHG) hydrogel with various dynamic properties, including injectability, shear-thinning and self-healing. The GHG hydrogel can be loaded with various therapeutic agents for a series of tissue regeneration. We first examined the skin regeneration of the GHG hydrogel-based wound dressing on a full-thickness burn mice model. Prolonged inflammatory response and insufficient vascularization cause delayed and poor wound healing. We demonstrated that the GHG hydrogel loaded with resveratrol and histatin-1 suppressed inflammation and promoted vascularization at skin burn wound sites. We next evaluated the efficacy of dynamic hydrogels to treat a debilitating injury, traumatic spinal cord injury. We demonstrated that the GHG hydrogel loaded with adipose-derived stromal cells promoted spinal cord regeneration via enhanced in-situ neurogenesis and efficient pro-healing immunomodulation. We next studied the efficacy of GHG hydrogels to promote osteochondral regeneration both in small and large animals. We demonstrated that the GHG hydrogel with tunable degradation kinetic supported effective hyaline cartilage repair in cartilage defect model of pig.

We then moved to utilize the engineered nanocomposite dynamic hydrogels mimicking the hierarchical biomechanical structures of the natural ECM. We demonstrated that the chemical incorporation of acryloyl nanoparticle-based cross-linkers creates regionally stiff network structures in the dynamic supramolecular hydrogels. The obtained dynamic hydrogels with a heterogeneous hydrogel network topology expedite the development of adhesion structures, 3D spreading, and mechanosensing of the encapsulated stem cells, as evidenced by the upregulated expression of key biomarkers such as vinculin, FAK, and YAP. This enhanced spreading and mechanotransduction promote the osteogenic differentiation of the encapsulated stem cells. In contrast, doping with physically entrapped nanoparticles or molecular cross-linkers (PEGDA) cannot locally reinforce the dynamic hydrogel network and therefore fails to facilitate cell mechanosensing or differentiation in the 3D hydrogels. We further show that the dynamic hydrogels with locally stiffened network promote the in-situ regeneration of bone defects in an animal model.

***** ALL ARE WELCOME *****

For enquiries, please contact Ms. Joyce Chan, Department of Biomedical Engineering at 3943 8278