The Chinese University of Hong Kong
Department of Biomedical Engineering

Graduate Seminar – PhD Oral Defence

Student : Mr. LI Zhuo
Supervisor : Prof. HO Yi Ping Megan
Date : 31 May 2022 (Tuesday)
Time : 2:00 pm
Zoom Link : https://cuhk.zoom.us/j/5877831498?pwd=cGUrejJkR2JDMW1QL21BcDR0R3dGdz09
Meeting ID : 5877831498
Password : 666888

Title: Dynamic hydrogels promote tissue regeneration through cellular metabolism and epigenetic regulation

Bone regeneration biomaterial scaffolds are the essential three-dimensional structure that supports diverse activities of cells to mediate tissue regeneration. Hydrogels, which closely resemble the highly hydrated and permeable extracellular matrix (ECM) of living tissues, have been widely adopted as tissue engineering scaffold. However, traditional hydrogels based on chemical crosslinking can limit the spreading, proliferation, cell – cell and cell – matrix interactions, and mechanosensing of encapsulated cells due to the highly static and restrictive network. Therefore, it is of great importance to develop hydrogels with dynamic structures to assist the basic and translation research in tissue engineer. We assembled a biomimetic hyaluronic acid nanocomposite hydrogel (HA-BP hydrogel) stabilized by the dynamic coordination bonds of bisphosphonates (BPs). Our HA-BP hydrogel can support the initial differentiation of primary macrophages to preosteoclasts, which is essential to bone regeneration, whereas further differentiation to mature osteoclasts is effectively inhibited by the HA-BP hydrogel via the acidity-triggered release of anti-osteoclastic bisphosphonate in a negative feedback fashion. Cellular energetics plays an important role in tissue regeneration, and enhanced metabolic activities can accelerate tissue regeneration. We fabricated a supramolecular hydrogel (HA-ADA) with high network dynamics based on the host – guest interaction between beta-cyclodextrin and adamantane (CD-ADA). Our studies showed that HA-ADA hydrogel enhanced the glucose uptake of encapsulated human mesenchymal stem cells (hMSCs) through glucose transporter 1 (GLUT1) activation compared with the hydrogel with low network dynamics. Furthermore, our HA-ADA hydrogel promoted lipid β-oxidation, TCA cycle, oxidative phosphorylation (OXPHOS), and ATP biosynthesis, thereby enhancing the energy supply to facilitate hMSC differentiation. Cellular metabolites are known to be transported into cell nucleus to mediate epigenetic modifications, such as m6A methylation, which is an important epigenetic event in regulating osteogenesis. We fabricated a highly dynamic hydrogel (HA-Cou) with double dynamic networks including dynamic acyl hydrazone bond and the host – guest interaction between γCD and coumarin. Our studies showed that HA-Cou hydrogel enhanced cell – cell interactions through E-Cadherin activation. In addition, our HA-Cou hydrogel promoted the energy sensor, AMPK and glucose transporter 1 (GLUT1), thereby enhancing TCA cycle. Furthermore, succinate generated from TCA cycle inhibited m6A demethylase, ALKBH5, relatively enhancing the METTL3-driven m^6A methylation.

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

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