# Augmenting Osteoporotic Bone Regeneration Through a Hydrogel-based Rejuvenating Microenvironment

**Xiaoting Zhang**

**Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, P. R. China**

**Email: zhangxiaoting@link.cuhk.edu.hk**

Osteoporotic bone defects pose a significant challenge for bone regeneration as they exhibit impaired healing capacity and delayed healing. To address this issue, this study introduces a hydrogel that creates a rejuvenating microenvironment, thereby facilitating efficient repair during the initial two weeks following surgery. The hydrogel, named GelHFS, was created through host-guest polymerization of gelatin and acrylated β-cyclodextrin. Incorporation of the human fetal mesenchymal stem cell (MSC) secretome formed GelHFS hydrogels aimed at mimicking a rejuvenated stem cell niche. Implantation of GelHFS in osteoporotic rat defects resulted in increased new bone formation at 2 weeks post implantation, compared to the GelCD hydrogel. GelHFS hydrogel recruited endogenous integrin β1-expressing cells and degraded according to the remodeling process in vivo. Also, our experiments demonstrated that GelHFS hydrogel promotes cell stellate spreading and osteogenic differentiation via integrin β1-induced focal adhesion pathway. Our findings reveal that GelHFS hydrogel provides a rejuvenating niche for endogenous MSCs and enhances bone regeneration in osteoporotic bone defects. These findings highlight the potential of GelHFS hydrogel as an effective therapeutic strategy for addressing impaired osteoporotic healing.

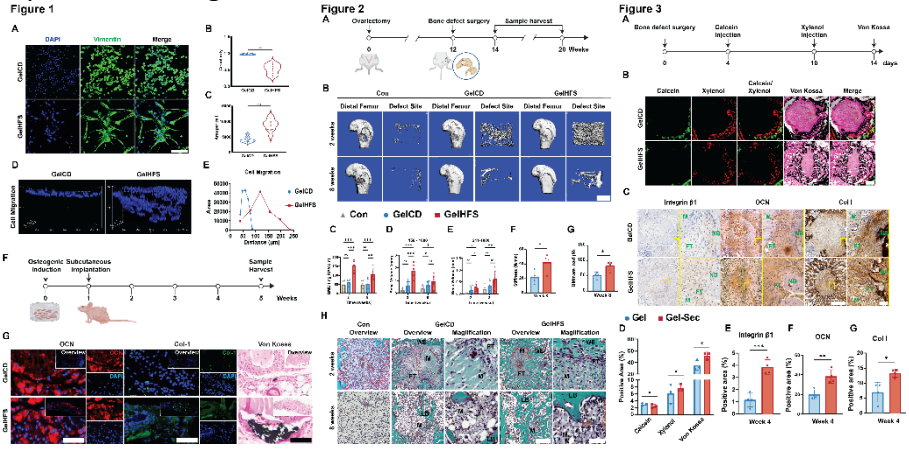


Figure 1. GelHFS hydrogel promotes spreading, migration and osteogenic differentiation of MSCs
Figure 2. GelHFS hydrogel enhances bone regeneration in osteoporotic model
Figure 3. GelHFS hydrogel recruits integrin β1+ cells into the defect site