# Department of Biomedical Engineering
# The Chinese University of Hong Kong

## Graduate Seminar – PhD Oral Defence

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| ***Student*** | ***:*** | Mr. WANG Yuwen |
| ***Supervisor*** | ***:*** | Prof. LI Zhong Alan |
| ***Date*** | ***:*** | 3 July 2026 |
| ***Time*** | ***:*** | 2:00pm |
| ***Venue*** | ***:*** | Room 1122, William M W Mong Engineering Building, CUHK |

**Title: Chiral Biomaterials for Modulating Stem Cell Fate and Enhancing Bone Regeneration**

Nanostructural chirality has emerged as a key design principle for regenerative biomaterials. However, how nanoscale chirality in biomaterials influences stem cell behavior and tissue regeneration remains poorly understood. This thesis hypothesizes that chiral nanomaterials—whether engineered nanoparticles or chiral-patterned surfaces—can regulate stem cell fate through enantiomer-selective interactions and activation of specific signaling pathways, thereby promoting bone healing.

Nanoparticles with defined chiral structures showed strong enantioselective effects on mesenchymal stem cells (MSCs). L-cysteinyl-L-phenylalanine nanoparticles (L-CF-NPs) exhibited significantly higher cellular uptake—through clathrin-mediated, integrin-dependent endocytosis—compared to other variants. This selective uptake led to the highest expression of osteogenic and pro-angiogenic genes and most robust mineralization of the MSCs, primarily through activation of MAPK/JNK/ERK signaling pathways. Incorporation of L-CF-NPs into volumetric 3D-bioprinted silk fibroin/gelatin methacryloyl (GelMA) scaffolds resulted in the fastest bone regeneration in a rat critical-size defect (CSBD) model.

In addition, nano-topographies with tailored chiral helices were fabricated to modulate the bioactivity of extracellular vesicles (EVs). Surfaces with left-handed helices promoted the generation of MSC-secreted EVs (LH-EVs) enriched with osteogenic and cellular metabolism-modulatory microRNAs. These EVs greatly enhanced the osteogenic differentiation of recipient MSCs, with underlying mechanisms involving the activation of MAPK and PI3K–AKT pathways as well as regulated cell energy metabolism mediated by AMPK. Delivery of these EVs using GelMA scaffolds dramatically improved new bone formation in a rat CSBD model.

Overall, these findings show that chiral biomaterials can effectively guide stem cell fate and enhance bone regeneration. By promoting enantioselective nanoparticle uptake and the secretion of highly bioactive EVs, chiral biomaterials offer promising platforms for both cell-based and cell-free bone repair strategies, with wider applications in regenerative medicine.

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

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