

Extracellular Matrix Biphasic Scaffold Synergizing Metformin and Kartogenin for Osteochondral Tissue Engineering

Chih-Hsiang Fang¹, Yi-Wen Lin², Jui-Sheng Sun^{1,3,*}

¹Department of Orthopedic Surgery, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 10002, Taiwan

²Institute of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University, No. 1, Sec. 4, Roosevelt Rd, Taipei 10617, Taiwan

³Department of Orthopedic Surgery, En Chu Kong Hospital, No. 399, Fuxing Rd., Sanxia Dist., New Taipei City, 237, Taiwan

Presenter: Chih-Hsiang Fang (danny07291991@hotmail.com)

Disclosures: Chih-Hsiang Fang (National Taiwan University Hospital), Yi-Wen Lin (National Taiwan University), and Jui-Sheng Sun (National Taiwan University Hospital and En Chu Kong Hospital)

INTRODUCTION: Osteoarthritis (OA) is a musculoskeletal disorder that is common in older adults and associated with high rates of morbidity. With limited durable treatments, mesenchymal stem cell (MSC)-based tissue engineering emerges as a potential regenerative strategy. Moreover, affordable and selective, small molecules drug can modify stem cell behavior during differentiation, holding promise for clinical use.

METHODS: This research introduced a biphasic scaffold (BPS) integrating a bone layer (gelatin/hydroxyapatite/metformin [GHSM]) and a cartilage layer (gelatin nano-fiber/kartogenin [NGFK]). The BPS, built on the extracellular matrix (ECM), was embedded with two small-molecule drugs, kartogenin (KGN) and metformin (MET), to drive osteochondral regeneration. Leveraging ECM-based biomaterials mirroring native tissues, the scaffold facilitated cell recruitment, infiltration, and differentiation without supplementary growth factors.

RESULTS SECTION: The BPS exhibited favorable in vitro biocompatibility. Mesenchymal stem cells (MSCs) displayed adherence, proliferation, and differentiation capabilities on both the GHSM and NGFK layers.

DISCUSSION: Co-culturing with NGFK and GHSM layers led to upregulation of double-stranded DNA (dsDNA), sulfated glycosaminoglycan (sGAG), as well as osteo- and chondrogenic biomarkers, alongside increased relative mRNA levels. Notably, histological staining indicated successful rat osteochondral defect regeneration in vivo.

SIGNIFICANCE/CLINICAL RELEVANCE: Anticipated to bolster subchondral bone healing and cartilage rejuvenation, this innovative biphasic scaffold demonstrates impressive abilities in fostering cell attraction and the enlistment of native cell populations.

IMAGES AND TABLES:

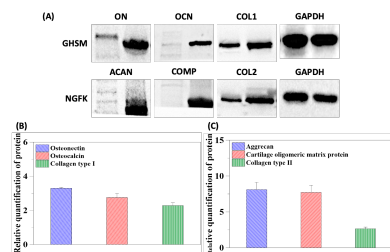


Figure 1. Relative osteogenic and chondrogenic gene expression in hMSCs cultured with the GHSM and NGFK, compared with the control group.

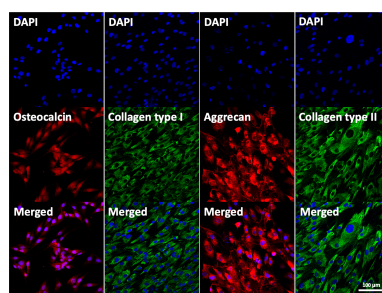


Figure 2. Immunofluorescence staining of osteo- and chondro-specific biomarkers. Osteocalcin and aggrecan were stained in red, and the different types of collagens were stained in green.

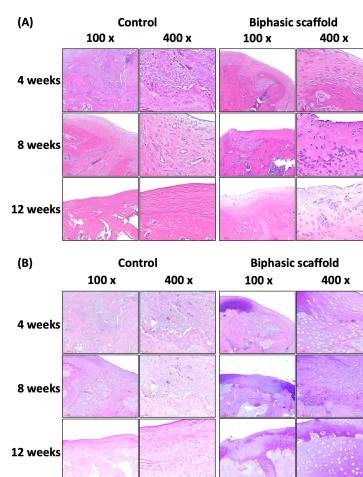


Figure 3. Histological staining. (A) H&E staining of subchondral bone. (B) AB/PAS staining of cartilage regeneration. The positive reaction between AB and PAS makes neutral and acidic mucocutaneous appear purple.