Osteochondral Tidemark Region Synthesis: Application of Siglec-15 Overexpression and Novel Seeded Hydrogel

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Musculoskeletal disorders include diverse complications but all suffer from the physiological orthopedic domino effect, namely bone mineral density (BMD) alterations. For instance, increased BMD of subchondral bone plates fosters osteoarthritis (OA) while in Fibrodysplasia Ossificans Progressiva (FOP), increased BMD triggers endochondral ossifications that induce cartilage degradation. To address ramifications of BMD and cartilage erosion, this study devised a synergistic therapy to (1) identify Sialic acid-binding Ig-like lectin 15's (Siglec-15) overexpression on osteoclast activity and (2) utilize a hydrogel scaffold (HS) construct to reconstitute tidemark interface and calcified cartilage zones (CCZ). Tartrate-resistant acid phosphatase (TRAP) staining measured para-nitrophenyl phosphate (PnPP) of Siglec-15 osteoclasts. Chondrocytes, bone chips, MSCs, and osteogenic media were cultured in HS to quantify Alcian Blue (AB) and Alizarin Red (AR) staining via ImageJ. TRAP staining revealed 3.77 + 0.17 μL and 2.27 + 0.20μL PnPP for Siglec-15 and vehicle osteoclasts. A non-parametric median test demonstrated that Siglec-15 osteoclasts exhibited a 60% increase in osteoclast activity relative to the vehicle group (*$p<0.05$). AB and AR staining confirmed 48.993% and 35.484% CCZ mineralization with osteogenic media and the control respectively. Thus, the Siglec-15 osteoclasts' enhanced resorptive ability and the MSC-seeded hydrogel's effective CCZ remodeling supported feasibility of interdisciplinary procedures to innovate an integrative tidemark interface. Future investigations include creating a sustainable physical scaffold for evaluation of the HS's biomechanical properties through unconfined compression tests and ImageJ analysis of Siglec-15 osteoclasts' resorption lacunas.

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