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CARTILAGE REPAIR IN VIVO USING EPIGENETIC REPROGRAMMING WITH SMALL MOLECULES

Muratkhodjaeva Saodat
Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan

Osteoarthritis (OA) is a progressive degenerative joint disease that significantly impairs mobility and quality of life, particularly in aging populations. Current therapeutic approaches primarily focus on symptom relief but fail to address the underlying mechanisms of cartilage degeneration. In recent years, epigenetic reprogramming has emerged as a promising strategy for cellular rejuvenation, offering new perspectives for regenerative medicine.

This study investigates the potential of a selected set of small chemical molecules (SCM) to induce epigenetic reprogramming of chondrocytes and promote cartilage regeneration in an in vivo model of chemically induced OA. The experiments were conducted on aging female rats, a translational model chosen for its relevance to human age-related OA and postmenopausal cartilage deterioration. OA was induced via intra-articular administration of trypsin, and a subset of animals was further subjected to estrogen receptor blockade using clomiphene citrate to simulate postmenopausal conditions. The SCM cocktail was administered intra-articularly to evaluate its effects on cartilage repair. Chondroitin sulfate was used as a comparative treatment control.

The results demonstrated that SCM administration led to significant improvements in joint tissue integrity, including increased cartilage thickness, enhanced synthesis of mucopolysaccharides, and restoration of chondrocyte metabolic activity. Histological analysis revealed that SCM-treated groups exhibited reduced cartilage erosion, lower inflammatory marker expression, and improved nuclear-cytoplasmic index (NCI) values, suggesting enhanced chondrocyte function. Notably, the group with estrogen receptor blockade responded more favorably to SCM treatment than the non-blocked OA group, highlighting the potential interaction between hormonal status and epigenetic reprogramming.

These findings provide strong evidence for the feasibility of epigenetic modulation as a therapeutic strategy for OA. The ability of SCMs to restore cartilage structure and function suggests a novel approach to treating age-related degenerative diseases. Further research is required to elucidate the precise molecular mechanisms underlying this rejuvenation process and optimize therapeutic protocols for clinical applications.