Osteoarthritis, aetiology, pathology and animal models

The ION CHANNEL TRPV4 PARTICIPATES IN THE CARTILAGE PROTECTION EFFECT OF IGURATIMOD ON KNEE OSTEOPATHY

**Keywords:** Cartilage, Disease-modifying drugs (DMARDs), Osteoarthritis

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**Background:** Osteoarthritis (OA) is the leading cause of disability for bone and joint diseases. Cartilage injury is its pathological basis. There is a lack of therapeutic drugs with clear cartilage protection in clinic. Iguratimod (IGU) has cartilage protection effect in the treatment of rheumatoid arthritis, but it is not clear whether it also has cartilage protection effect on OA.

**Objectives:** To investigate the efficacy and mechanism of Iguratimod (IGU) on cartilage protection effect on knee osteoarthritis (OA).

**Methods:** Type II collagenase was injected into the knee joint cavity of C57BL/6/N rats to establish a model of CIAO (Collagenase-induced Osteoarthritis), to establish a model of OA, followed by IGU given by intragastrum at 10mg/kg. μCT and Immunohistochemistry (IHC) were used to evaluate the structural changes of OA knee joint, the degree of destruction of knee cartilage layer and subchondral bone. IHC and qPCR were used to evaluate the expression of TRPV4 in chondrocytes of OA rats. Chondrocytes were processed by IGU at the cellular level, and the concentration of glycosaminoglycan secreted and the expression of chondrogenic differentiation factor in chondrocytes were further detected. TRPV4 ion channel inhibitor and interfering RNA technology were used to verify whether TRPV4 was involved in the effect of IGU on cartilage.

**Results:** It was found that IGU could change the pain sensitivity of OA model rats and effectively reduce the pain of OA rats. qPCR showed that IGU could effectively inhibit the subchondral bone injury of knee joint in OA rats, Tolidine blue staining and Safranin O-Fast Green staining of rats knee joint also showed that IGU treatment could delay the degeneration of cartilage in rats with OA. At the cellular level, it was found by qPCR that IGU could effectively promote the expression of mRNA levels of Sox9 and Col2a, markers of chondrogenesis, in chondrocytes. Alcian blue staining also showed that IGU promoted chondrocyte secretion of glycosaminoglycan; Moreover, the results of scratch experiment also showed that IGU promoted the migration of chondrocytes. The results addressed above all indicated that IGU could promote the differentiation of chondrocytes.

**Conclusion:** IGU can effectively alleviate the pain of OA model rats, and exert cartilage protection by regulating TRPV4. The results offer new treatment options for osteoarthritis.

**REFERENCES:** NIL.

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