An intra-articular injection of FGF-2 induced proliferative reaction in mouse knee joints

Purpose: Fibroblast growth factor-2 (FGF-2) is one of the candidates to regenerate articular cartilage tissue due to the potent effects on chondrocytes. In order to consider FGF-2 for such clinical use, it is necessary to understand how FGF-2 influences on articular joints in vivo. An intra-articular injection of human recombinant FGF-2 into mouse knee joints was performed, and the following changes were investigated.

Materials and methods 1) An intra-articular injection of radiolabeled FGF-2 in order to examine on which cells the injected FGF-2 molecules was attached. Human recombinant FGF-2 was obtained from Sios Nova, Ca, USA. Iodination of FGF-2 was performed using a chloramine-T. The radiolabeled FGF-2 (0.25 μCi of 2.5 μg in 5 μl of PBS) was injected through the patellar tendon into the right knee joints of C57Bl/10 mice (10 weeks old). The injected knee joint was harvested two, four or 72 hours after the injection. The sections of the harvested specimens were developed and then fixed followed by back staining with HE. 2) An intra-articular injection of FGF-2 in order to examine the effects on the articular joint. Various doses of FGF-2 in 5 μl of PBS or control solution of BSA (5 μg) was injected as described above. The injected knee joints were harvested 7, 14, or 21 days after the injection. Coronal sections were stained with safranin-O for histological analysis. Articular cartilage proteoglycan content is measured using an image analysis for safranin-O staining intensity in histological sections. It was normalized with the density of the growth plate cartilage of the same section.

Results: Four hours after an injection of radiolabeled FGF-2, radio-positive cells were detected in the superficial and radial zones of the articular cartilage as well as in the synovium and perichondrium adjacent to the articular cartilage. An injection of FGF-2 (5 μg) caused synovial hyperplasia and perichondrial cell proliferation on day 7. Chondrocyte formation adjacent to the articular cartilage was observed on day 14, and it was matured as osteophyte with articular surface on day 21. Additionally, intensity of safranin-O staining of the articular cartilage increased significantly on day 14 and 21. On the contrary, low dose of FGF-2 (40ng) or control injections did not show histological changes.

Conclusion: An intra-articular injection of FGF-2 stimulated proliferative reaction of the chondroprogenitor cells in the synovium or perichondrium followed by osteocyte formation, and matrix synthesis of the articular cartilage.