

the other antibodies. It is reported that the structure of guinea pig IGF-1 is similar to that of human IGF-1 (LeRoith et al., 1993). In this study, we used anti-human IGF-1 antibody and anti-human IGF-1 receptor antibody for detection of IGF-1 and IGF-1 receptor of guinea pig.

Results

Based on the histological-histochemical grading system, five 1- to 5-month-old animals were classified as the mild group. The mean osteoarthritis grade was 0.60 ± 0.89 . Seven 3- to 8-month-old animals were included in the moderate group, with a mean osteoarthritis grade of 5.14 ± 1.77 . Five 8- to 18-month-old animals comprised the severe group, with a mean osteoarthritis grade of 9.40 ± 0.89 .

Histopathological findings

Mild group (grades 0–2)

When articular cartilage of the medial condyle of the tibia in the mild group was examined, fibrous connective tissue continuous with the synovial membrane and covering the margins of the articular cartilage was observed at the synovium-cartilage junction in all animals. Fibrous connective tissue at this junction was not stained with safranin O. In the most superficial layer of the fibrous connective tissue at the junction, fibroblastic-like cells were present almost continuously from superficial cells of the synovial membrane. In a layer deeper than these fibroblastic-like cells, chondrocytes were observed, but these were not clustered. Osteophyte formation was not noted in any animal (Fig. 1A).

In the weight-bearing regions of the cartilage of animals showing osteoarthritis changes, a rougher structure of the superficial layer, slight proliferation of chondrocytes, and slightly decreased safranin-O staining intensity were noted.

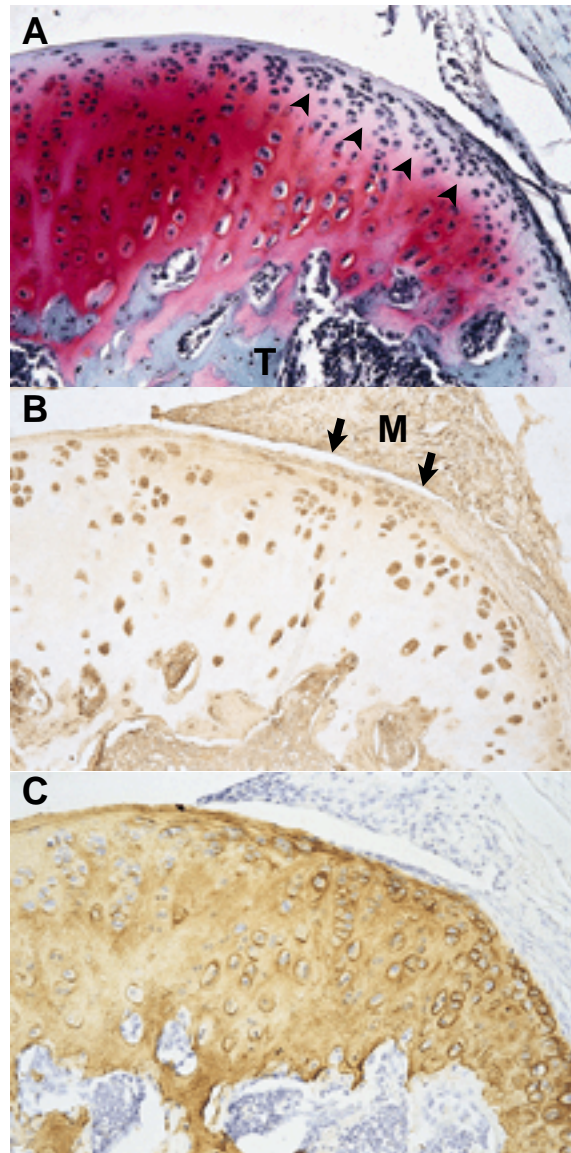
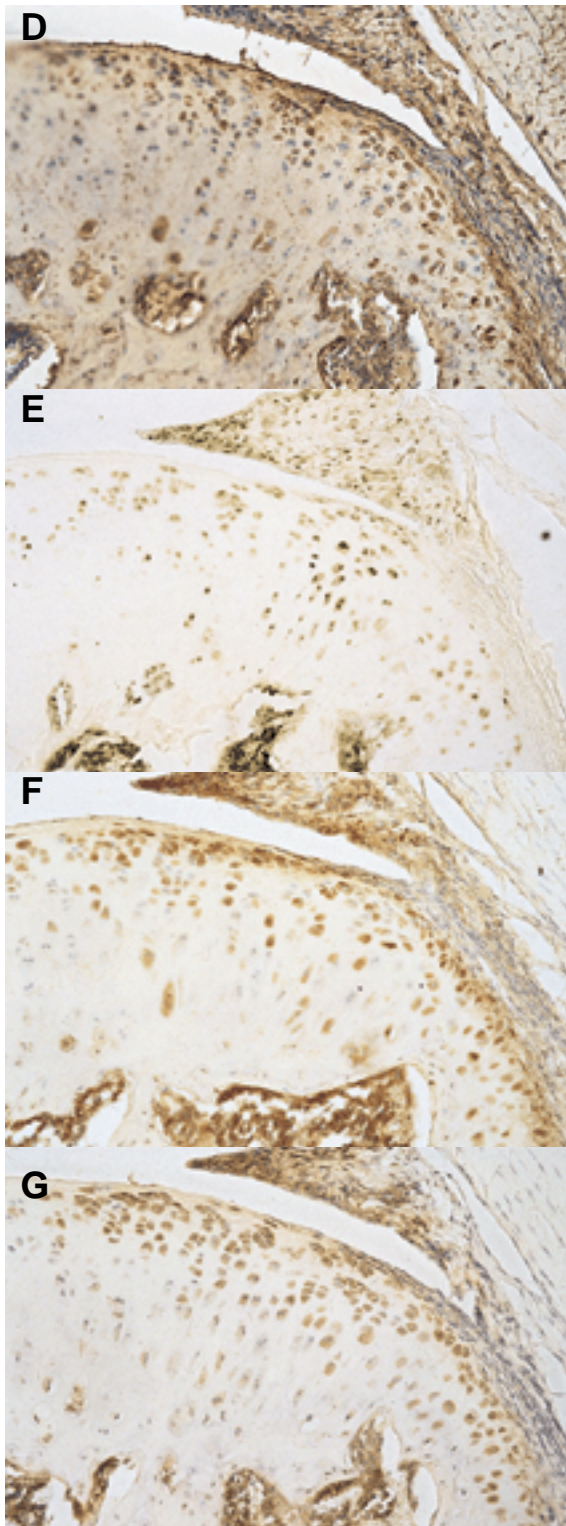


Fig. 2. Chondrocytes (arrowheads) cluster in a layer deeper than fibroblastic-like cells in the fibrous connective tissue (arrows) in the moderate group of 3-month-old animals, in which degenerative changes had progressed further (A, B). These chondrocytes, which are negative for type-I and -III collagens and PCNA in the mild group, are positive for all (B, D, E respectively) in the moderate group. This staining pattern is similar to that of fibroblastic-like cells in the fibrous connective tissue. Around these chondrocytes, cartilage matrix positive for type-II collagen is recognized (C). IGF-1 (F) and IGF-1 receptor (G) are identified in fibroblastic-like cells and chondrocytes seen in a layer deeper than the fibroblastic-like cells. M, medial meniscus; T, tibia. Original magnification, $\times 200$. [Figs. 2A–C on p. 134; Figs. 2D–G on p. 135]



Figs. 2D–G. *Continued from the previous page.*

Moderate group (grades 3–7)

In the moderate group in which cartilage degeneration had progressed further, cells similar to chondrocytes had clustered in a layer below fibroblastic-like cells near the superficial layer of the margins of the articular cartilage. These cells had less cytoplasm. Chondrocyte formation was noted in 1 animal and osteophyte formation in another (Fig. 2A).

The weight-bearing regions of the cartilage showed fissures extending to the transitional zone and moderate to marked reduction in safranin-O staining intensity. The number of chondrocytes was decreased.

Severe group (grades 8–13)

A chondrocyte was identified in 1 animal (Fig. 3A) and osteophytes in 4 animals. Fibrous connective tissue of the synovium-cartilage junction and fibroblastic-like cells were noted around the osteophyte. Chondrocytes were recognized near the boundary between the osteophyte and weight-bearing regions of the cartilage, but had not clustered (Fig. 4A).

Fissures from the radial zone to the calcified zone and markedly reduced safranin-O staining intensity were noted in the weight-bearing regions of the cartilage. The number of chondrocytes was noticeably decreased.

Synovial membrane

The lining cells of the synovium consisted of 2 to 4 layers and proliferated more with osteoarthritis progression, but there were no findings suggestive of synovitis, such as villous formation or cell infiltration into sublining synovial tissue.

Immunohistological staining

Mild group

At the margins of the articular cartilage, the cytoplasm of fibroblastic-like cells in the fibrous connective tissue was positive for type-I (Fig. 1B) and -III (Fig. 1D) col