INTRODUCTION
Surgery or trauma around the joints or tendons frequently brings about adhesions, which cause severe functional impairments. Adhesion formation is essentially a fibrogenetic process, and several studies have suggested that growth factors such as TGF-β play a central role in its development. Therefore, suppression of the cytokine’s activity could decrease adhesions. It has recently been found that many proteoglycans function as modulators of growth factors. Among them, small proteoglycan decorin was demonstrated to neutralize the activity of TGF-β. Decorin can thus be expected to be an inhibitor of adhesions. The purpose of this study was to test this hypothesis using an intra-articular adhesion model in rabbits.

MATERIALS AND METHODS
Twenty male, mature Japanese white rabbits, weighing 3.1 to 3.6 Kg, were used for this study. They were randomly divided into 4 groups of 5 rabbits, and intra-articular adhesion was developed as follows. Both medial and lateral sides of the right femoral condyle were exposed, cortical bone was removed in a defined area (10x5 mm) and underlying cancellous bone was exposed. Two polyethylene tube were fixed at both sides of the condyle, which were connected each to the two osseous mini pumps (Alert 2MJA, Alza, Palo Alto, CA) implanted under the skin in the abdomen. Decorin (Sigma Chemical, St. Louis, MO) was suspended in PBS and supplied continuously through these tubes. After the surgery, the right knee joint was immobilized in the fully flexed position with a fiberglass cast from groin to foot for 4 weeks. The left leg was left untreated.

Decorin was administered in 2 groups: in one group, the administration rate was 4µg/24 hrs (Group 1), and in the other group, it was 22 µg/24 hrs (Group 2). The remaining two groups were used as the controls: in one, no solution was administered (Control 1), and in the other, bovine serum albumin PBS solution was administered at the rate of 22µg/24 hrs (Control 2). Four weeks after the surgery, the animals were sacrificed and casts were taken off gently. Immediately thereafter, lateral view radiographs were taken under a determined extension torque of 4.9 Nm, and the angles of flexion contracture of the knee joints (FAs) were determined on these films. Thus the adhesions were evaluated biomechanically. Following the roentgenography, right knee joints were opened and adhesions developed between the lateral femoral condyles and lateral joint capsules were macroscopically observed. Subsequently, 30 mg wet weight of the adhesion tissue was obtained from the decorticated area in the lateral femoral condyle, and total collagen content was determined on the basis of hydroxyproline concentration.

All the animal experiments were performed at the University of Tokyo under the approval of the institutional review board. Statistical analysis was performed with one-way factorial ANOVA and Dunnett’s multiple comparison test as a post-hoc test, and p<0.05 was set as significant.

RESULTS
In Control 1, FAs ranged from 65 to 81 degrees, which showed an adequate reproducibility of our model. There was no significant difference in FAs between Control 1 and Control 2. The decorin groups both had significantly smaller FAs in comparison with Control 1 (Group 1, p<0.05; Group 2, p<0.01). Fig. 1. Macroscopic observation showed that the adhesions were looser and weaker in the decorin groups. Biochemical analyses further supported these results, demonstrating that collagen content decreased with the administration of decorin. The angles of flexion contractures of the knee joints in the decorin groups were significantly lower from those of Control 1 (p<0.01). Fig. 2.

DISCUSSION
The results of this study demonstrated that locally administered decorin could reduce adhesion formation, probably by decreasing collagen accumulation. This was quite reasonable as a consequence of the inhibition of TGF-β activity, because this cytokine is known to be a potent stimulator of extracellular matrix synthesis. Recently, it has been suggested that use of TGF-β antagonist may be a promising approach to various pathologies with tissue fibrosis (2). In the field of orthopaedics, however, this study might be a precedent report on TGF-β antagonist (1). Decorin can thus be expected to be an inhibitor of adhesions. This study might be a precedent report on TGF-β antagonist (1). Decorin can thus be expected to be an inhibitor of adhesions. This study might be a precedent report on TGF-β antagonist (1). Decorin can thus be expected to be an inhibitor of adhesions. This study might be a precedent report on TGF-β antagonist (1). Decorin can thus be expected to be an inhibitor of adhesions. This study might be a precedent report on TGF-β antagonist (1). Decorin can thus be expected to be an inhibitor of adhesions. This study might be a precedent report on TGF-β antagonist (1). Decorin can thus be expected to be an inhibitor of adhesions. This study might be a precedent report on TGF-

REFERENCES:

ACKNOWLEDGMENT: This work was supported financially in part by the Grant-in-Aids for General Scientific Research (No.08671640) from the Ministry of Education, Science and Culture in Japan.

PROTEOGLYCAN DECORIN REDUCES FORMATION OF ADHESION THROUGH THE SUPPRESSION OF COLLAGEN OVERPRODUCTION

*Fukui, N., Nakajima, K., Tashiro, T., Hiraksa, H., Oda, H., Nakamura, K. +*Department of Orthopaedic Surgery, The University of Tokyo. Hongo 7-3-1, Bunkyo-ku, Tokyo 113-0033, Japan: +81-3-3815-5411, EXT3376, FAX +81-3-3818-4082

PC 8 ABSTRACT NO. 1404


One or more of the authors have received something of value from a commercial or other party related directly or indirectly to the subject of my presentation.

The authors have not received anything of value from a commercial or other party related directly or indirectly to the subject of my presentation.