Introduction

One of the essential pathomechanisms of the age-related degeneration of intervertebral discs is a loss of proteoglycan in nucleus pulposus (NP). However, the regulatory mechanisms of proteoglycan synthesis/accumulation involved in the metabolism of intervertebral discs remains unresolved, especially its relationship to age. Transforming growth factor-β1 (TGF-β1) is a potent regulator of the growth/differentiation and matrix synthesis of many types of cells including those of chondrogenic lineage. The effects of TGF-β1 on the actions of cells derived from intervertebral discs have been reported. However, the actual expression of this growth factor and its receptors in intervertebral discs and the age-dependent effect of TGF-β1 on disc cells have never been investigated.

Materials and Methods

The present study investigates the expression of TGF-β1 and its receptors by disc cells and age-related changes using 8-, 40-, and 120-week-old rat. We also examine age-related changes in TGF-β1-dependent proteoglycan synthesis, using cultured cells derived from rat intervertebral discs. Tissues and cells were separately harvested from NP and anulus fibrosus (AF) to examine the individual characteristics of the cells derived from different components of intervertebral discs.

Results

Semi-quantitative RT-PCR analysis indicated that the level of gene expression of TGF-β1/TGF-β1 receptor type I (TβR-I) of NP decreased with age. In AF, the level of TGF-β1/TβRs gene expression did not apparently differ with age. Consistent with the RT-PCR results, stimulation of proteoglycan synthesis by TGF-β1 in NP cells decreased with age. Proteoglycan synthesis by AF cells was also stimulated by TGF-β1. However, levels of this stimulation by AF cells were identical.

Discussion

The present findings indicate that the genetic expression of TGF-β1/TβR-I and TGF-β1-dependent proteoglycan synthesis decreased with age in NP cells, and further suggest that a loss of proteoglycan synthesis with age in the intervertebral disc is at least due to the transcriptional down regulation of TGF-β1/TβR-I and decreased synthetic ability of proteoglycans in response to TGF-β1 by NP cells. All the current findings suggest a mechanism of age-dependent proteoglycan loss from intervertebral discs which is a common feature of the elderly. The mechanism clarified in this study is explained as a decrease in the ability of NP cells to synthesize TGF-β1 with increasing age together with age-related decreases in TGF-β1-dependent proteoglycan synthesis by disc cells, possibly via a TβR-I pathway. This notion may help to resolve the problems underlying degenerative spinal disorders, and to generate novel means of preventing and/or treating intervertebral disc diseases.