INTRODUCTION
Low back pain (LBP) associated with degenerative disc disease (DDD) is a global health problem affecting millions of people and carries significant socio-economic impact [1]. Generally, the homeostasis of IVD is maintained by the balance between the anabolism and catabolism of disc cells. This balance is regulated by a variety of factors, such as growth factors, cytokines, enzymes and their inhibitors. Currently, clinical therapeutic treatment for IVD includes attempts to biochemically up-regulate the major components of extracellular matrix (e.g., aggrecan, collagen type II) and/or anabolic factors (e.g., tissue inhibitor of metalloproteinase), or to down-regulated the expression of catabolic enzymes (e.g., metalloproteinase, aggrecanases) the expressions of which are up-regulated by various catabolic cytokines and growth factors, including interleukin-1, tumor necrosis factor-alpha, and basic fibroblast growth factor.

Bovine lactoferricin (LfcinB) is a cationic peptide that shows cytotoxic activity against microorganisms, viruses, and various human cancer cells. LfcinB, containing the N-terminal sequence of lactoferrin, is composed of 25 amino acid residues and is originated by acidic pepsin hydrolysis. The anti-inflammatory, antioxidant, anti-pain, and anticancer properties of LfcinB have already been well reported [2]. More recently, natural antioxidants have been reported to provide a protective effect on articular cartilage. However, it is not known if LfcinB exerts similar protective effects in degenerating IVDs.

Therefore, the aim of the present study is to determine the potential of LfcinB in regaining the progression of IVD degeneration. Specifically, we studied the effect of LfcinB on IVD homeostasis by assessing the gene expression levels of catabolic genes and anabolic genes, PG accumulation, PG synthesis, and signaling transduction in the IVD.

METHODS
IVD tissue was obtained from bovine coccygeal tissue of 15-18 months old bovine disc. Chondrocytes were isolated from bovine nucleus pulposus, digested by pronase and collagenase, and plated on 12-well plate at 8X10^6 cells/cm² in a 1:1 mixture of DMEM/ Ham’s F12 medium containing 10% FBS. Chondrocytes cultured in serum free media were stimulated with LfcinB or/and chemicals for 24hrs. After cultivation, chondrocytes were harvested for real-time PCR or western blot.

The anabolic action and signal transduction of Lactoferricin in the intervertebral disc

As shown in Fig. 1C, ECM was increased by LfcinB treatment, compared with control. These data suggest that Lfcin B can be enhanced anabolism in the homeostasis of IVD.

RESULTS
The chondrocytes stimulated with LfcinB for 21 days significantly increased PG accumulation in a dose-dependent manner (Fig. 1A). To determine if the increase in PG accumulation was mediated by LfcinB-induced stimulation of PG synthesis, the incorporation of 35S-sulfate by chondrocyte into PGs was quantified.

DISCUSSION
Here we demonstrate the anabolic and anti-catabolic effect of LfcinB via the p38 MAPK signaling pathways. According to previous studies, SP1, which is the downstream target transcriptional factor of p38 MAPK activation, stimulates the transcriptional expression of aggrecan and TIMP3 in the presence of TGF-beta in chondrocytes [2-3]. Therefore, being similar to TGF-beta, a well known anabolic growth factor for cartilage, Lfcin B might be an excellent candidate for treatment of disc degeneration.

REFERENCES

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