INTRODUCTION:
Decoy receptor 3 (DcR3)/TR6/M68 is a member of the tumor necrosis factor receptor (TNFR) superfamily. DcR3 lacks the transmembrane domain of conventional TNFRs to be a secreted protein. DcR3 is overexpressed in a variety of tumors, including lung and colon cancers, gliomas, gastrointestinal tract tumors, autoimmune tissues, and virus-associated leukemia. Over expression of DcR3 might benefit tumors by helping them avoid cytotoxic and regulatory effects of FasL, LIGHT, and TL1A. Meanwhile, osteoarthritis (OA) is the most common degenerative disease of human articular cartilage. It is characterised by extracellular matrix damage and an important loss in tissue cellularity. Apoptosis, or programmed cell death, is a physiological process for maintaining homeostasis in both embryogenic and adult tissue but may also have a role in diseases involving articular cartilage degeneration, such as OA. Hence, we speculated that DcR3 might contribute to the pathogenesis of OA by down-regulating apoptosis in OA chondrocyte. In this study, we investigated DcR3 expression in OA cartilage and analyzed the function of DcR3 to Fas induced apoptosis, and suggested DcR3 as a novel therapeutic intervention in OA therapy.

MATERIALS AND METHODS:
Expression of DcR3 in OA and normal cartilage
Cartilage tissues were obtained during knee arthroplasty from patients with osteoarthritides and femoral neck fracture (normal cartilage). Chondrocytes were obtained from the cartilage tissues and cultured. All experiments were conducted using the cells of first passage.

Pre-treatment of chondrocytes with DcR3 protein before apoptosis induction
Before the induction of apoptosis, chondrocytes were pre-treated with 0.1, 1, 10 and 100 ng/ml of recombinant human DcR3-Fc protein for 24h.

Fas-induced apoptosis in cultured chondrocytes
Apoptosis in OA chondrocytes was induced by human recombinant FasL (100ng/ml) for 12h.

Detection of apoptosis
Apoptosis was detected with TUNEL method and immunoblotting of cleaved caspase 8 and cleaved PARP (Poly(ADP) ribose polymerase).

Proliferation assay
Chondrocytes were incubated with various stimulations, and proliferation of chondrocytes were analysed by ZTT assay.

RESULTS:
1) DcR3 was expressed in cartilage tissues.
DcR3 was dominantly expressed in deep zone of cartilage tissues by immunohistochemistry (Fig. 1a), and DcR3 mRNA was multicopied in cultured chondrocytes (Fig. 1b). Realtime-PCR showed that the expression levels of DcR3 mRNA have not significantly differences between OA and normal chondrocytes (Fig. 1b).

2) DcR3 protein inhibited Fas-induced apoptosis in OA chondrocytes.
TUNEL positive apoptotic cells induced by Fas-L in chondrocytes were significantly decreased in a dose dependent manner when chondrocytes were pre-incubated with DcR3-Fc protein (Fig. 2a). Cleavage of caspase 8 and PARP was also significantly decreased (Fig. 2b).

3) DcR3 stimulates chondrocytes proliferation
Proliferation assay revealed that the growth rates of chondrocytes were significantly increased by the treatments with least 1 ng/ml of DcR3-Fc protein in control (Fig. 3a), and the growth rates of chondrocytes were significantly increased by the treatments with least 100 ng/ml of DcR3-Fc protein when apoptosis were introduced by Fas-ligand (Fig. 3b).

CONCLUSION:
DcR3 was expressed in cartilage tissues and chondrocytes. DcR3-Fc protein inhibited Fas-induced apoptosis in RA-FLS. DcR3-Fc induced chondrocytes proliferation. In conclusion, DcR3 contributes to apoptosis and proliferation in OA cartilage tissues.