**Introduction:** Rheumatoid Arthritis (RA) is an auto-immune disease characterized by over proliferation of synovial tissues and following joint destruction. Rheumatoid synovium are composed with two types of synoviocytes, macrophage-like synoviocytes and fibroblast-like synoviocytes (FLS) [1]. We previously reported that decoy receptor 3 (DcR3), a secreted decoy tumor necrosis factor receptor competitively binding to Fas-ligand, LIGHT, and TL1A, is overexpressed in RA-FLS when stimulated with TNFα and protects the cells from Fas-induced apoptosis [2]. We investigated the expression of DcR3 in THP-1 monocytes/macrophages and analyzed the function of DcR3 for the regulation of cell adhesion and apoptosis in the macrophages.

**Materials and Method:** Monocyte to macrophage differentiation. Human mononcic THP-1 cells (1 to 2×10⁶/ml) were incubated with 5ng/ml PMA, 10ng/ml hTNFα, 1ng/ml hIL-6, hTNFα and hIL-6, 10ng/ml LPS, 3μg/ml DcR3-Fc, or 3μg/ml human IgG1 for 24 h. Quantification of mRNA expression. The relative levels of mRNA encoding adhesion molecules in THP-1 cells were compared by real-time PCR. Cell aggregation. Aggregate formation was investigated by photomicrograph. Western blotting. Cycloheximide(CHX)-induced apoptotic signals were confirmed by detection of full-length and poly (ADP-ribose) polymerase (PARP), caspase 3, and caspase 9. Pre-treatment of THP-1 cells with DcR3-Fc. THP-1 cells were incubated with 3μg/ml of DcR3-Fc for 24 h before apoptosis is induced by CHX for 12 h. Pre-treatment of THP-1 cells with anti-VLA-4 Ab or IgG1 before PMA or DcR3-Fc stimulation. THP-1 cells were pre-incubated with either anti-VLA-4 mAb or control IgG1 for 2 h prior to the treatment with PMA or DcR3-Fc. TUNEL staining. Apoptotic cells were determined using TUNEL assay kit.

**Results:** DcR3 mRNA was increased when THP-1 cells were induced to differentiate by PMA, but not by TNFα or TNFβ and IL-6 (data not shown). Concurrently, the aggregate formation of differentiated macrophages was observed when differentiated by PMA, but not by TNFα or TNFβ and IL-6 (data not shown). Real-time PCR showed that only integrin α4 mRNA expression was significantly increased in THP-1 cells stimulated with DcR3-Fc among the various integrins (Fig. 1). The aggregate formation of differentiated macrophages was also observed when stimulated with DcR3-Fc. Cells were induced to differentiate with TNFα and IL-6 (panel a-f) followed by the incubation with no stimulation (panel a), 1μg/ml IgG1 (panel b), 3μg/ml DcR3-Fc (panel c), 1μg/ml DcR3-Fc (panel d), 3μg/ml DcR3-Fc (panel e), or PMA (panel f) (Fig. 2A). Even undifferentiated THP-1 cells were induced to form aggregates by DcR3-Fc. Cells were photographed after 24h incubation with no stimulation (panel a), 1μg/ml IgG1 (panel b), 3μg/ml DcR3-Fc (panel c), 1μg/ml DcR3-Fc (panel d), 3μg/ml DcR3-Fc (panel e), or PMA (panel f) (Fig. 2B). TUNEL positive apoptotic cells induced by CHX in THP-1 macrophages were significantly decreased when pre-incubated with DcR3-Fc (Fig. 3B). Meanwhile, when the cells are induced to apoptosis by CHX, cleavage of PARP was inhibited when THP-1 cells were pre-treated with TNFα and IL-6, PMA, or DcR3-Fc (Fig. 3C). Inhibition of TUNEL-positive apoptosis of CHX-treated THP-1 cells by DcR3-Fc was significantly decreased by anti-VLA4 Ab, but not by IgG1 (Fig. 4A). Inhibition of cleavage of PARP, caspase 3, and caspase 9 in CHX-treated THP-1 cells by DcR3-Fc was also significantly decreased by anti-VLA4 Ab, but not by IgG1 (Fig. 4B).

**Discussion:** In this study, we showed that integrin α4 expression was increased in THP-1 cells and cell aggregates were formed by DcR3-Fc. Further, CHX-induced apoptosis was inhibited by DcR3-Fc. Both the inhibition of CHX-induced apoptosis and the aggregate formation by DcR3-Fc were ameliorated by anti-VLA-4 Ab. Previous studies have revealed that VLA-4 is significantly increased in rheumatoid synovium and these adhesion molecules play a role in the regulation of inflammation [3]. Hence, our results suggest that DcR3 protects the macrophages from apoptosis by increasing integrin α4 and inhibiting the aggregate formation. In conclusion, we suggest that DcR3 may play a significant role in macrophages not only by a decoy receptor but also by increasing α4 integrin. By regulating the proliferation and migration of macrophages via α4 integrin, DcR3 might contribute to the pathogenesis of RA.